

Jan Delaval please

Access DB# 67522

## SEARCH REQUEST FORM

Scientific and Technical Information Center

Requester's Full Name: Sabita Qazi Examiner #: 74141 Date: 5/25/02  
Art Unit: 1616 Phone Number 305-3910 Serial Number: 09/893,324  
Mail Box and Bldg/Room Location: 2019, 011 Results Format Preferred (circle): PAPER DISK E-MAIL  
3807

If more than one search is submitted, please prioritize searches in order of need.

\*\*\*\*\*

Please provide a detailed statement of the search topic, and describe as specifically as possible the subject matter to be searched. Include the elected species or structures, keywords, synonyms, acronyms, and registry numbers, and combine with the concept or utility of the invention. Define any terms that may have a special meaning. Give examples or relevant citations, authors, etc, if known. Please attach a copy of the cover sheet, pertinent claims, and abstract.

Title of Invention: Alkyl ether modified polycyclic compds  
having a terminal phenyl + uses

Inventors (please provide full names): Prokai et al.

Earliest Priority Filing Date: 6/27/01

\*For Sequence Searches Only\* Please include all pertinent information (parent, child, divisional, or issued patent numbers) along with the appropriate serial number.

Please search for a steroidal compd  
where ring A is unsaturated and  
containing an alkyl ether at 17 position  
of D ring.  
e.g. 1,3,5(10) triene -3-ol-17-alkyl ether  
estradiol.

Please see attached sheet

Thank you

Jan Delaval  
Reference Librarian  
Biotechnology & Chemical Library  
CM1 1E07 - 703-308-4498  
jan.delaval@uspto.gov

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### STAFF USE ONLY

Searcher: Qazi  
Searcher Phone #: 4498  
Searcher Location: \_\_\_\_\_  
Date Searcher Picked Up: 5/29/02  
Date Completed: 5/29/02  
Searcher Prep & Review Time: \_\_\_\_\_  
Clerical Prep Time: 15  
Online Time: 740

### Type of Search

NA Sequence (#) \_\_\_\_\_  
AA Sequence (#) ✓  
Structure (#) \_\_\_\_\_  
Bibliographic \_\_\_\_\_  
Litigation \_\_\_\_\_  
Fulltext \_\_\_\_\_  
Patent Family \_\_\_\_\_  
Other \_\_\_\_\_

### Vendors and cost where applicable

STN \_\_\_\_\_  
Dialog \_\_\_\_\_  
Questel/Orbit \_\_\_\_\_  
Dr.Link \_\_\_\_\_  
Lexis/Nexis \_\_\_\_\_  
Sequence Systems ✓  
WWW/Internet \_\_\_\_\_  
Other (specify) \_\_\_\_\_

=> fil reg

FILE 'REGISTRY' ENTERED AT 11:20:53 ON 29 MAY 2002  
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STRUCTURE FILE UPDATES: 27 MAY 2002 HIGHEST RN 422267-53-6  
DICTIONARY FILE UPDATES: 27 MAY 2002 HIGHEST RN 422267-53-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

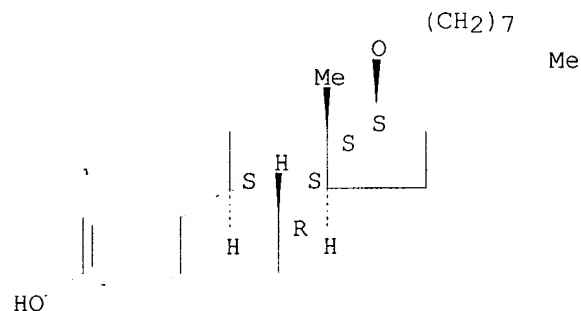
Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS  
Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d ide can tot l21

L21 ANSWER 1 OF 5 REGISTRY COPYRIGHT 2002 ACS  
RN 319427-07-1 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 17-(octyloxy)-, (17.beta.)- (9CI) (CA INDEX  
NAME)  
FS STEREOSEARCH  
MF C26 H40 O2  
SR CA  
LC STN Files: CA, CAPLUS, TOXCENTER, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1967 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

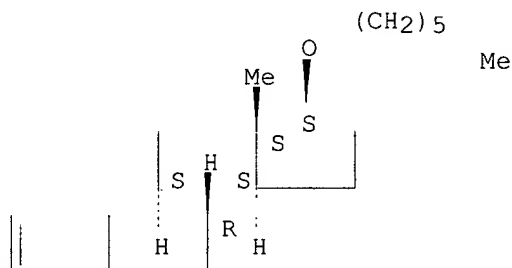
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REFERENCE 2: 135:221441  
REFERENCE 3: 134:101056

L21 ANSWER 2 OF 5 REGISTRY COPYRIGHT 2002 ACS  
RN 319427-06-0 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 17-(hexyloxy)-, (17.beta.)- (9CI) (CA INDEX  
NAME)

Jan Delaval  
Reference Librarian  
Biotechnology & Chemical Library  
CM1 1E07 - 703-308-4498  
[jan.delaval@uspto.gov](mailto:jan.delaval@uspto.gov)

FS STEREOSEARCH  
 MF C24 H36 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

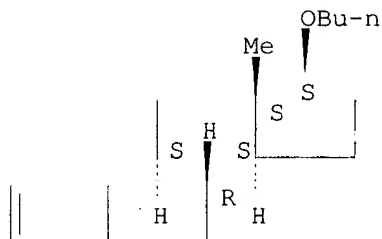
2 REFERENCES IN FILE CA (1967 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:85991

REFERENCE 2: 134:101056

L21 ANSWER 3 OF 5 REGISTRY COPYRIGHT 2002 ACS  
 RN 319427-05-9 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 17-butoxy-, (17.beta.)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C22 H32 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

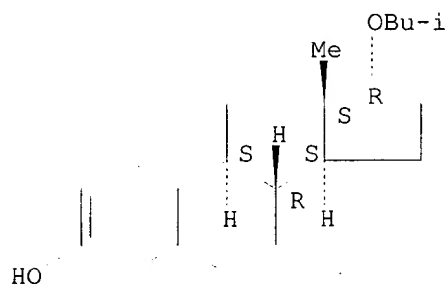
REFERENCE 1: 136:85991

REFERENCE 2: 134:101056

L21 ANSWER 4 OF 5 REGISTRY COPYRIGHT 2002 ACS

RN 119309-39-6 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 17-(2-methylpropoxy)-, (17.alpha.)- (9CI) (CA INDEX NAME)  
OTHER NAMES:  
CN 17.alpha.-Isobutylestradiol  
FS STEREOSEARCH  
MF C22 H32 O2  
SR CA  
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

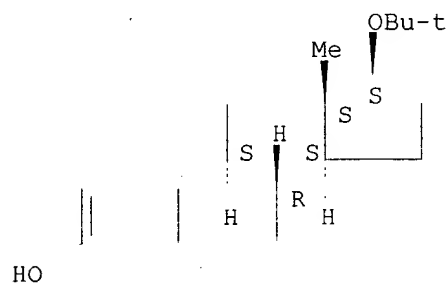
2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 113:29367

REFERENCE 2: 110:121535

L21 ANSWER 5 OF 5 REGISTRY COPYRIGHT 2002 ACS  
RN 38781-59-8 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 17-(1,1-dimethylethoxy)-, (17.beta.)- (9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C22 H32 O2  
LC STN Files: BEILSTEIN\*, CA, CAPLUS  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1967 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 85:154233

REFERENCE 2: 80:121187

REFERENCE 3: 77:101990

=> d his 121-

(FILE 'REGISTRY' ENTERED AT 11:12:06 ON 29 MAY 2002)

L21 5 S L15,L20

SEL RN

L22 0 S E19-E23/CRN

FILE 'HCAOLD' ENTERED AT 11:20:06 ON 29 MAY 2002

L23 0 S L21

FILE 'USPATFULL, USPAT2' ENTERED AT 11:20:07 ON 29 MAY 2002

L24 1 S L21

FILE 'HCAPLUS' ENTERED AT 11:20:18 ON 29 MAY 2002

L25 8 S L21

L26 3 S L1-L3 AND L25

L27 8 S L25,L26

FILE 'REGISTRY' ENTERED AT 11:20:53 ON 29 MAY 2002

=> fil uspatall

FILE 'USPATFULL' ENTERED AT 11:21:06 ON 29 MAY 2002

CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 11:21:06 ON 29 MAY 2002

CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> d 124 bib abs hitstr

L24 ANSWER 1 OF 1 USPATFULL

AN 2002:61264 USPATFULL

TI Alkyl ether modified polycyclic compounds having a terminal phenol and  
uses for protection of cells

IN Prokai, Laszlo, Gainesville, FL, UNITED STATES

Simpkins, James W., Fort Worth, TX, UNITED STATES

PI US 2002035100 A1 20020321

AI US 2001-893324 A1 20010627 (9)

PRAI US 2000-214077P 20000627 (60)

DT Utility

FS APPLICATION

LREP BROMBERG & SUNSTEIN LLP, 125 SUMMER STREET, BOSTON, MA, 02110-1618

CLMN Number of Claims: 46

ECL Exemplary Claim: 1

DRWN 5 Drawing Page(s)

LN.CNT 951

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and compositions are provided for achieving a cytoprotective effect by selecting a polycyclic compound with a phenol group at one end of the molecule and a carbon ring at the other such that an alkyl ether functional group in which the alkyl group has a formula  $C_{sub}H_{sub}nH_{sub}2n+1$  (where n is at least 3 and less than 20) is positioned on the carbon ring. The compound may be used to achieve a cytoprotective effect in cells and to retard the development of a degenerative condition in a subject suffering from a disease, trauma or aging.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

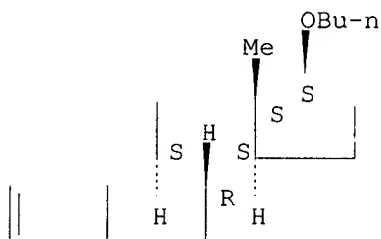
IT 319427-05-9P

(crystal structure)

RN 319427-05-9 USPATFULL

CN Estra-1,3,5(10)-trien-3-ol, 17-butoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

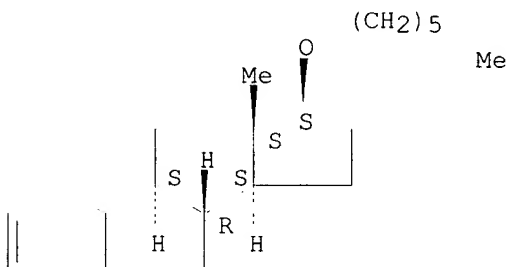
IT 319427-06-0P 319427-07-1P

(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)

RN 319427-06-0 USPATFULL

CN Estra-1,3,5(10)-trien-3-ol, 17-(hexyloxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

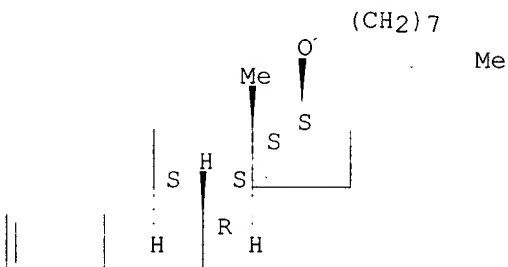


HO

RN 319427-07-1 USPATFULL

CN Estra-1,3,5(10)-trien-3-ol, 17-(octyloxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

=&gt; fil hcaplus

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FILE COVERS 1907 - 29 May 2002 VOL 136 ISS 22  
FILE LAST UPDATED: 27 May 2002 (20020527/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

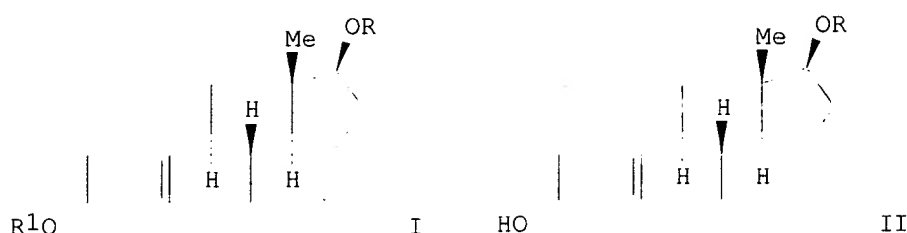
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L27 ANSWER 1 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
AN 2002:10439 HCAPLUS  
DN 136:85991  
TI Preparation of 17.beta.-alkyl ether estradiol derivatives with cytoprotective activity of cells from degeneration through disease, trauma or aging  
IN Prokai, Laszlo; Simpkins, James W.  
PA University of Florida Research Foundation, Inc., USA  
SO PCT Int. Appl., 29 pp.  
CODEN: PIXXD2  
DT Patent  
LA English  
IC ICM C07D  
CC 32-3 (Steroids)  
Section cross-reference(s): 1, 75

FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | WO 2002000619   | A2   | 20020103 | WO 2001-US41170 | 20010627 |
|      | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM |      |          |                 |          |
|      | RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG  |      |          |                 |          |
|      | US 2002035100   | A1   | 20020321 | US 2001-893324  | 20010627 |
| PRAI | US 2000-214077P   | P    | 20000627 |                 |          |

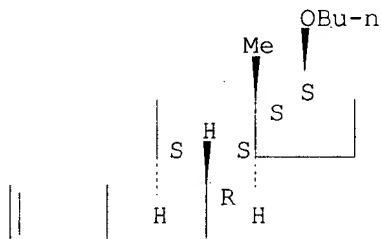
GI



- AB Cytoprotective compds. I (R = Me, Et, Pr, Bu, (CH<sub>2</sub>)<sub>5</sub>Me, or (CH<sub>2</sub>)<sub>7</sub>Me; R<sub>1</sub> = OH) were prepd. in 50-75% yields from 17.β.-estradiol. 17.β.-Estradiol and benzyl halide in K<sub>2</sub>CO<sub>3</sub> gave 93% yield of 3-benzyloxyestra-1,3,5(10)-trien-17.β.-ol which was then alkylated with the appropriate alkyl halides in DMF and NaH yielding the 3-benzyloxy protected derivs. of I which were then deprotected via catalytic hydrogenation using ammonium formate in Pd/C. Thus compds. II (R = hexyl and octyl) were prepd. in 70 and 75% resp., and were neuroprotective to a similar extent at a concn. of 10 .μM and 1 .μM. Typical compns. contain approx. 0.01-95% by wt. of active ingredient and the percentage of active ingredient will depend upon the dosage form and mode of administration; an ED of the active agent as measured in the plasma of a subject may be in the range of 5pg/mL-5000pg/mL. Cytoprotective compds. I (R = OH; R<sub>1</sub> = Bu, (CH<sub>2</sub>)<sub>7</sub>Me) were prepd. from 17.β.-estradiol and Bu or octyl bromide in K<sub>2</sub>CO<sub>3</sub> in 68 and 72% resp.
- ST estradiol hydroxy alkylated deriv prepn cytoprotective compn; neuroprotective alkyl ether steroid prepn; crystal structure butoxyestratrienol
- IT Steroids, preparation  
 RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (alkylation of 17.β.-OH or 3-OH; prepn. of 17.β.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Cytoprotective agents  
 (cardioprotective; prepn. of 17.β.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Nervous system  
 (degeneration; prepn. of 17.β.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Alkylation  
 (hydroxyalkylation; prepn. of 17.β.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Eye, disease  
 (macula, degeneration; prepn. of 17.β.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Crystal structure  
 (of 17.β.-butoxyestra-1,3,5(10)-trien-3-ol)
- IT Estrogen receptors  
 RL: BSU (Biological study, unclassified); BIOL (Biological study)  
 (prepn. of 17.β.- or 3-alkyl ether derivs. of estradiol used as cytoprotective agents of cells from degeneration)
- IT Anti-Alzheimer's agents  
 Anti-ischemic agents  
 Bone, disease  
 Drug delivery systems  
 (prepn. of 17.β.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Osteoporosis  
 (therapeutic agents; prepn. of 17.β.- or 3-alkyl ether derivs. of

- estradiol used for cytoprotective activity of cells from degeneration)
- IT **319427-05-9P**  
 RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (crystal structure)
- IT 4954-12-5P 21830-24-0P 128805-68-5P 319427-03-7P 319427-04-8P  
**319427-06-0P 319427-07-1P**  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT 50-28-2, 17.beta.-Estradiol, reactions 109-65-9, Butyl bromide 111-83-1, Octyl bromide  
 RL: RCT (Reactant); RACT (Reactant or reagent)  
 (prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT 14982-15-1P 141318-37-8P 319426-98-7P 319426-99-8P 319427-00-4P 319427-01-5P 319427-02-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
 (prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT **319427-05-9P**  
 RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (crystal structure)
- RN 319427-05-9 HCAPLUS
- CN Estra-1,3,5(10)-trien-3-ol, 17-butoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

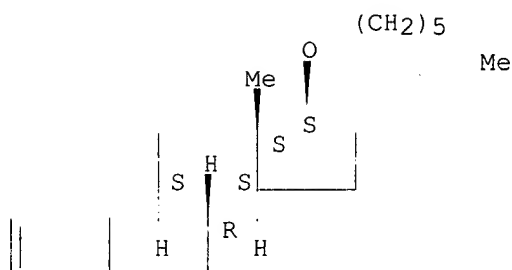
Absolute stereochemistry.



HO

- IT **319427-06-0P 319427-07-1P**  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
 (prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- RN 319427-06-0 HCAPLUS
- CN Estra-1,3,5(10)-trien-3-ol, 17-(hexyloxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

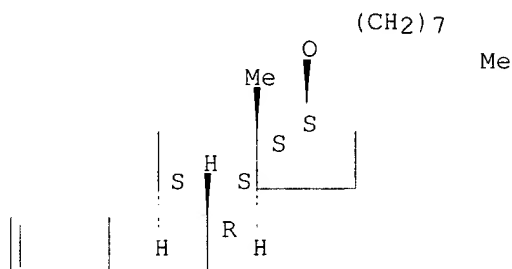


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RN 319427-07-1 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-(octyloxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L27 ANSWER 2 OF 8 HCAPLUS COPYRIGHT 2002 ACS

AN 2001:428147 HCAPLUS

DN 135:221441

TI Membrane fluidity effects of estratrienes

AU Liang, Y.; Belford, S.; Tang, F.; Prokai, L.; Simpkins, J. W.; Hughes, J. A.

CS Department of Pharmaceutics, University of Florida, Gainesville, FL, USA

SO Brain Research Bulletin (2001), 54(6), 661-668

CODEN: BRBUDU; ISSN: 0361-9230

PB Elsevier Science Inc.

DT Journal

LA English

CC 2-4 (Mammalian Hormones)

AB Estrogens have demonstrable neuroprotective effects. This fact has lead to the proposed use of estrogens for the prevention and/or treatment of Alzheimer's disease. The exact protective mechanism estrogens provide is not fully understood. In this report, a potential non-genomic mechanism for estratrienes involving alterations in membrane fluidity was studied. Steroids, such as estrogen, are known to be membrane-active and can alter the lipid packing. In this study the authors used fluorescent methodologies to address the effect of naturally occurring steroids (17.alpha.- and 17.beta.-estradiol, testosterone, and progesterone) and new estratriene analogs on membrane fluidity using liposomes and HT-22 hippocampal cells. The study's results indicate steroids, based on the estratriene nucleus, can modulate lipid packing as evidenced by (1) decreased membrane fusion events and (2) decreased membrane fluidity. The effects on the membrane were both time- and concn.-dependent. It was also demonstrated through rational design.estratriene analogs can be synthesized with enhanced membrane effects. Finally, in a

- glutamate-induced toxicity HT-22 model, the authors also demonstrated cellular protection with the estratriene-based mols. and analogs. The data suggest the plethora of cellular actions of estrogens may relate to or be influenced by membrane effects of the steroid.
- ST cell membrane fluidity estratriene; estradiol membrane fluidity
- IT Animal cell line  
(HT-22; estratrienes effects on membrane fluidity)
- IT Membrane, biological  
(bilayer; estratrienes effects on membrane fluidity)
- IT Liposomes  
(estratrienes effects on membrane fluidity)
- IT Phosphatidylethanolamines, biological studies  
Phosphatidylserines  
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(estratrienes effects on membrane fluidity)
- IT Brain  
(hippocampus; estratrienes effects on membrane fluidity)
- IT 57-88-5, Cholesterol, biological studies  
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)  
(estratrienes effects on membrane fluidity)
- IT 50-28-2, 17.beta.-Estradiol, biological studies 53-63-4,  
Estra-1,3,5(10)-trien-3-ol 57-83-0, Progesterone, biological studies  
57-91-0, 17.alpha.-Estradiol 58-22-0, Testosterone  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)  
(estratrienes effects on membrane fluidity)
- IT **319427-07-1P**  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(estratrienes effects on membrane fluidity)
- IT 50-50-0, 17.beta.-Estradiol 3-benzoate  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(estratrienes effects on membrane fluidity)

RE.CNT 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD  
RE

- (1) Abrami, L; J Cell Biol 1999, V147, P175 HCAPLUS
- (2) Behl, C; Biochem Biophys Res Commun 1995, V216, P473 HCAPLUS
- (3) Behl, C; Int J Vitam Nutr Res 1999, V69, P213 HCAPLUS
- (4) Behl, C; Prog Neurobiol 1999, V57, P301 HCAPLUS
- (5) Bodor, N; J Am Chem Soc 1989, V111, P3783 HCAPLUS
- (6) Cowley, S; J Biol Chem 1997, V272(2), P19858
- (7) Davy, A; J Neurochem 2000, V74, P676 HCAPLUS
- (8) Dewar, M; J Am Chem Soc 1985, V107, P3902 HCAPLUS
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- (12) Gridley, K; Mol Pharmacol 1998, V54, P874 HCAPLUS
- (13) Gu, Q; J Physiol 1998, V506, P745 HCAPLUS
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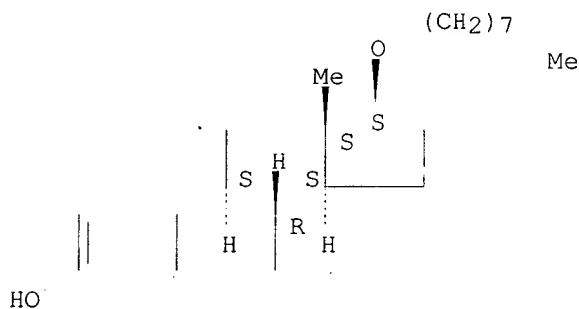
IT 319427-07-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(estratrienes effects on membrane fluidity)

RN 319427-07-1 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-(octyloxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L27 ANSWER 3 OF 8 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:820327 HCAPLUS

DN 134:101056

TI Synthesis and Biological Evaluation of 17.beta.-Alkoxyestra-1,3,5(10)-trienes as Potential Neuroprotectants Against Oxidative Stress

AU Prokai, Laszlo; Oon, Su-Min; Prokai-Tatrai, Katalin; Abboud, Khalil A.; Simpkins, James W.

CS Center for Drug Discovery College of Pharmacy Department of Anesthesiology College of Medicine and Center for Neurobiology of Aging College of Pharmacy, University of Florida, Gainesville, FL, 32610-0497, USA

SO Journal of Medicinal Chemistry (2001), 44(1), 110-114  
CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

CC 32-3 (Steroids)

Section cross-reference(s): 1, 75

OS CASREACT 134:101056

AB 17.beta.-O-Alkyl ethers (Me, Et, Pr, Bu, hexyl, and octyl) of estradiol were obtained from 3-O-benzyl-17.beta.-estradiol with sodium hydride/alkyl halide, followed by the removal of the O-benzyl protecting group via catalytic transfer hydrogenation. An increase compared to estradiol in the protection of neural (HT-22) cells against oxidative stress due to exposure of glutamate was furnished by higher (C-3 to C-8) alkyl ethers, while Me and Et ethers decreased the neuroprotective effect significantly. Lipophilic (Bu and octyl) ethers blocking the phenolic hydroxyl (3-OH) of A-ring were inactive.

ST alkoxyestratriene prepn neuroprotectant oxidative stress; estratriene alkoxy prepn neuroprotectant oxidative stress

IT Cytoprotective agents  
(neuroprotectants; synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT Crystal structure  
Molecular structure  
Oxidative stress, biological  
(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT Estrogens  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT 319427-05-9P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT 4954-12-5P 21830-24-0P 128805-68-5P 319427-03-7P 319427-04-8P  
319427-06-0P 319427-07-1P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT 50-28-2, 17.beta.-Estradiol, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT 14982-15-1P 141318-37-8P 319426-98-7P 319426-99-8P 319427-00-4P  
319427-01-5P 319427-02-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 319427-05-9P

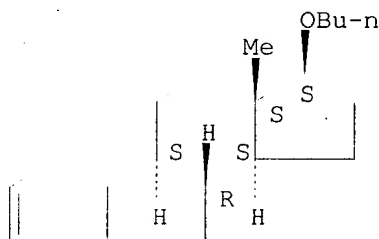
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

RN 319427-05-9 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-butoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

IT 319427-06-0P 319427-07-1P

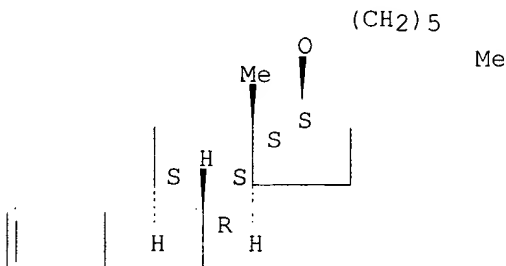
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

RN 319427-06-0 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-(hexyloxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

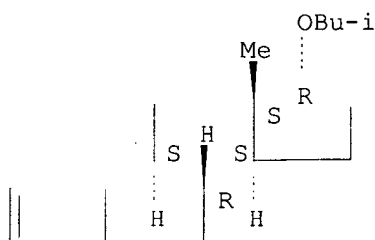
Absolute stereochemistry.



HO

(impurities detn. in, by HPLC)  
 IT 119309-39-6, 17.alpha.-Isobutylestradiol  
 RL: ANT (Analyte); ANST (Analytical study)  
 (detn. of, in ethynylestradiol by HPLC)  
 RN 119309-39-6 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(2-methylpropoxy)-, (17.alpha.)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.

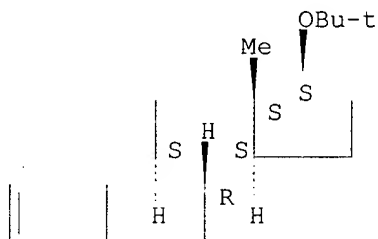


HO

L27 ANSWER 6 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1976:554233 HCAPLUS  
 DN 85:154233  
 TI Study of the specificity of the estradiol-binding system of guinea pig  
 uteri  
 AU Shchedrina, R. N.; Sturchak, S. V.; Bobrova, E. G.; Ishkov, V. L.;  
 Pivnitskii, K. K.; Fanchenko, N. D.  
 CS All-Union Res. Inst. Obstet. Gynecol., Moscow, USSR  
 SO Byull. Eksp. Biol. Med. (1976), 82(8), 989-93  
 CODEN: BEBMAE  
 DT Journal  
 LA Russian  
 CC 2-3 (Hormone Pharmacology)  
 AB The affinities of 49 steroids for the estradiol [50-28-2]-binding system  
 of guinea pig uteri were compared. The presence of free OH groups in  
 positions 3 (phenol) and 17.beta. and reciprocal orientation were required  
 for interaction with the receptor system. An intact steroid skeleton was  
 not necessary. A polar function in ring C inhibited interaction. In  
 addn. to estradiol, 17.alpha.-ethynylestradiol [57-63-6], synestrol, and  
 diethylstilbestrol [56-53-1] had high affinities for the estradiol-binding  
 system.  
 ST estradiol receptor interaction estrane deriv  
 IT Uterus, metabolism  
 (estradiol binding by, estrane derivs. in relation to)  
 IT Receptors  
 RL: BIOL (Biological study)  
 (for estradiol, of uterus, estrane derivs. interaction with)  
 IT Estrane, derivs.  
 RL: BIOL (Biological study)  
 (estradiol binding system of uterus interaction with)  
 IT 50-27-1 50-50-0 53-16-7 53-45-2 53-63-4 56-53-1 57-63-6  
 72-33-3 84-16-2 90-15-3 113-38-2 900-83-4 963-75-7 979-32-8  
 1035-77-4 1089-78-7 1125-78-6 1217-09-0 1624-62-0 1630-83-7  
 1852-96-6 2299-08-3 2529-64-8 2639-53-4 3736-22-9 6218-29-7  
 14550-57-3 15833-07-5 19590-55-7 32436-64-9 32436-65-0  
 32436-66-1 34124-99-7 38781-59-8 39662-38-9 40481-16-1  
 54064-57-2 54064-60-7 54064-61-8 58395-78-1 60779-03-5  
 60779-04-6 60779-05-7 60779-06-8 60788-62-7 60812-06-8  
 60827-74-9 60872-64-2  
 RL: BIOL (Biological study)

(estradiol binding system of uterus interaction with)  
 IT 50-28-2, biological studies  
 RL: BIOL (Biological study)  
 (uterus binding of)  
 IT 38781-59-8  
 RL: BIOL (Biological study)  
 (estradiol binding system of uterus interaction with)  
 RN 38781-59-8 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(1,1-dimethylethoxy)-, (17.beta.)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.

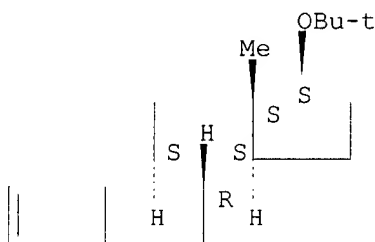


HO

L27 ANSWER 7 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1974:121187 HCAPLUS  
 DN 80:121187  
 TI Replacing the phenol hydroxy group with hydrogen. Reductive cleavage of alkyl esters of estrogens by lithium in ethers  
 AU Cherkasov, A. N.; Golubovskaya, L. E.; Pivnitskii, K. K.  
 CS Inst. Eksp. Endokrinol. Khim. Gorm., Moscow, USSR  
 SO Zh. Org. Khim. (1974), 10(2), 320-8  
 CODEN: ZORKAE  
 DT Journal  
 LA Russian  
 CC 32-3 (Steroids)  
 GI For diagram(s), see printed CA Issue.  
 AB The estratrienol ether I (R = Me3CO) was refluxed in an Ar atm. in glyme contg. Li to give I (R = HO). Under the same conditions I (R = MeOCH2O, tetrahydro-2H-pyran-2-yloxy) yielded I (R = H), and I (R = MeO, Me2CHO) gave a mixt. of I (R = H, HO). Analogous cleavage products were obtained from estradiol and estrone ethers.  
 ST estratrienol ether cleavage; alkoxyestratriene ether cleavage  
 IT Steroids, reactions  
 RL: RCT (Reactant)  
 (3-alkoxy-1,3,5(10)-unsatd., reductive cleavage of)  
 IT 50-28-2, reactions  
 RL: RCT (Reactant)  
 (etherification of)  
 IT 53-16-7  
 RL: RCT (Reactant)  
 (ketalization and etherification of)  
 IT 38781-61-2P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 IT 75-26-3 107-30-2  
 RL: RCT (Reactant)  
 (reaction of, with estratrienol)  
 IT 53-63-4  
 RL: RCT (Reactant)  
 (reaction of, with isopropylbromide)

IT 1852-96-6 3589-91-1 38781-54-3 38781-59-8 52509-95-2  
 52509-96-3 52509-97-4 52610-62-5  
 RL: RCT (Reactant)  
 (reductive cleavage of)  
 IT 115-11-7, reactions  
 RL: RCT (Reactant)  
 (with estratrienol)  
 IT 38781-59-8  
 RL: RCT (Reactant)  
 (reductive cleavage of)  
 RN 38781-59-8 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(1,1-dimethylethoxy)-, (17.beta.)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.

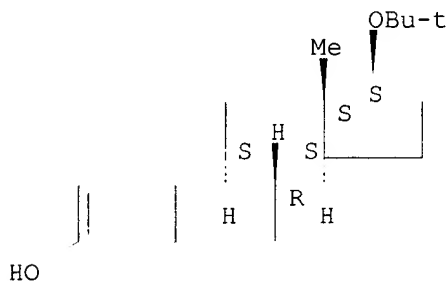


HO

L27 ANSWER 8 OF 8 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1972:501990 HCAPLUS  
 DN 77:101990  
 TI New method for the replacement of phenolic hydroxyl group by hydrogen.  
 Reduction of alkoxyalkyl ethers of phenols by lithium  
 AU Cherkasov, A. N.; Pivnitskii, K. K.  
 CS Inst. Eksp. Endokrinol. Khim. Gorm., Moscow, USSR  
 SO Zh. Org. Khim. (1972), 8(1), 211-12  
 CODEN: ZORKAE  
 DT Journal  
 LA Russian  
 CC 32-3 (Steroids)  
 AB 3-(Methoxymethoxy)estrane and the tetrahydropyranyl ethers of estranol, estranediol, and estrone ethylene ketal were reduced by finely divided Li in refluxing MeOCH<sub>2</sub>CH<sub>2</sub>OMe to the corresponding 3-H compds. in 76-91% yield. The tert-Bu ethers of estranol and estranediol gave the corresponding phenols in 75-98% yields, resp., under identical conditions.  
 ST lithium redn steroidal phenol; alkoxyalkoxy steroid redn; dehydroxylation phenol steroidal  
 IT Steroids, reactions  
 RL: RCT (Reactant)  
 ((alkoxyalkoxy), dealkoxylation of by lithium)  
 IT Dealkoxylation  
 (of (alkoxyalkoxy) steroids, by lithium)  
 IT 1217-09-0P 38781-61-2P 38781-62-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 IT 53-63-4 1852-96-6 3589-91-1 14550-57-3 38781-53-2 38781-54-3  
 38781-56-5 38781-57-6 38781-59-8  
 RL: RCT (Reactant)  
 (reaction of, with lithium)  
 IT 7439-93-2, reactions  
 RL: RCT (Reactant)  
 (with (alkoxyalkoxy)estrane derivs.)

IT 38781-59-8  
 RL: RCT (Reactant)  
 (reaction of, with lithium)  
 RN 38781-59-8 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(1,1-dimethylethoxy)-, (17.beta.)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



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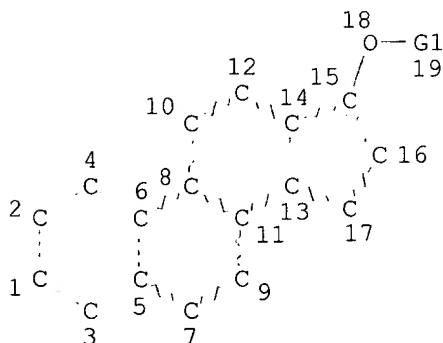
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Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
 for more information. See STNote 27, Searching Properties in the CAS  
 Registry File, for complete details:  
<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=> d sta que l32

L30 STR



VAR G1=AK/CB  
 NODE ATTRIBUTES:  
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DEFAULT ECLEVEL IS LIMITED

GRAPH ATTRIBUTES:

RSPEC 5

NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

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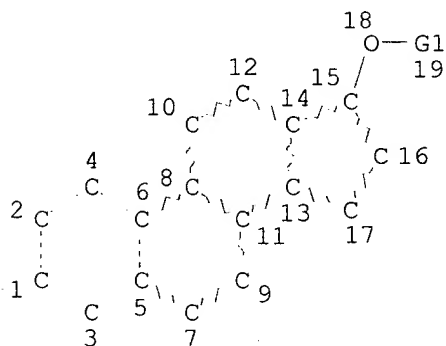
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L30 STR



VAR G1=AK/CB

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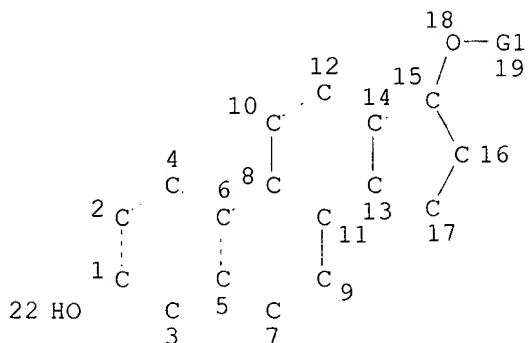
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NUMBER OF NODES IS 19

STEREO ATTRIBUTES: NONE

L32 4506 SEA FILE=REGISTRY SSS FUL L30

L49 STR



Ak @20 Cb @21

VAR G1=20/21

NODE ATTRIBUTES:

CONNECT IS M1 RC AT 14

DEFAULT MLEVEL IS ATOM

DEFAULT ECLEVEL IS LIMITED

ECOUNT IS M3 C AT 20

ECOUNT IS M3 C AT 21

## GRAPH ATTRIBUTES:

RSPEC 5

NUMBER OF NODES IS 22

## STEREO ATTRIBUTES: NONE

L51 15 SEA FILE=REGISTRY SUB=L32 CSS FUL L49

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15 ANSWERS

SEARCH TIME: 00.00.01

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FILE 'HCAPLUS' ENTERED AT 11:09:34 ON 29 MAY 2002

E PROKAI L/AU

L1 89 S E3,E4

L2 1 S E7

E SIMPKINS J/AU

L3 227 S E3,E5,E7-E9

L4 22 S L1-L3 AND STERO?/SC,SX,CW

L5 123 S L1-L3 AND (?ESTROGEN? OR ?ESTRADIOL? OR ?STEROID?)

L6 126 S L4,L5

L7 8 S L1,L2 AND L3

L8 3 S L7 AND L4-L6

L9 0 S L6 AND ALKYLETHER

L10 2 S L6 AND ALKYL(L)ETHER

L11 2 S L10 AND L1-L10

SEL RN

FILE 'REGISTRY' ENTERED AT 11:12:06 ON 29 MAY 2002

L12 18 S E1-E18

L13 16 S L12 AND NR&gt;=4

L14 5 S L13 AND (C22H32O2 OR C24H36O2 OR C26H40O2)

L15 3 S L14 NOT 3() (BUTOXY OR OCTYLOXY)

L16 777 S (C22H32O2 OR C24H36O2 OR C26H40O2)/MF AND C5-C6-C6-C6/ES

L17 110 S L16 AND 4432.3.65/RID AND 4/NR

L18 104 S L17 NOT 3 OL

L19 6 S L17 NOT L18

L20 5 S L19 NOT 13C#

L21 5 S L15,L20

SEL RN

L22 0 S E19-E23/CRN

FILE 'HCAOLD' ENTERED AT 11:20:06 ON 29 MAY 2002

L23 0 S L21

FILE 'USPATFULL, USPAT2' ENTERED AT 11:20:07 ON 29 MAY 2002

L24 1 S L21

FILE 'HCAPLUS' ENTERED AT 11:20:18 ON 29 MAY 2002

L25 8 S L21

L26 3 S L1-L3 AND L25

L27 8 S L25,L26

FILE 'REGISTRY' ENTERED AT 11:20:53 ON 29 MAY 2002

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FILE 'HCAPLUS' ENTERED AT 11:21:16 ON 29 MAY 2002

FILE 'REGISTRY' ENTERED AT 11:21:39 ON 29 MAY 2002

L28 STR  
L29 0 S L28 SAM  
L30 STR L28  
L31 21 S L30 SAM  
L32 4506 S L30 FUL  
SAV TEMP L32 QAZI893324/A  
L33 3917 S L32 AND 4432.3.65/RID  
L34 589 S L32 NOT L33  
L35 STR L28  
L36 5 S L35 CSS SAM SUB=L32  
L37 642 S L32 NOT ESTRA?  
L38 314 S L37 NOT ?PREGN?/CNS  
L39 86 S L38 NOT GONA?  
L40 48 S L39 NOT CHOL?  
L41 3864 S L32 NOT L37-L40  
L42 3 S L32 NOT CN/FA  
L43 5 S L35 CSS SAM SUB=L41  
L44 100 S L35 CSS FUL SUB=L41  
SAV TEMP L44 QAZI893324A/A  
L45 95 S L44 NOT L21  
L46 93 S L45 NOT (ION OR LABELED OR (D OR T)/ELS OR 11C# OR 13C# OR 14  
L47 22 S L46 AND 4/NR  
L48 3 S L47 AND (C21H28O2 OR C21H26O2 OR C21H30O2)  
L49 STR L35  
L50 0 S L49 CSS SAM SUB=L32  
L51 15 S L49 CSS FUL SUB=L32  
SAV L51 TEMP QAZI893324B/A  
L52 13 S L51 NOT (13C# OR T/ELS)  
L53 8 S L48,L52 NOT L21

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L54 0 S L53

FILE 'HCAPLUS' ENTERED AT 11:38:36 ON 29 MAY 2002

L55 10 S L53

FILE 'USPATFULL, USPAT2' ENTERED AT 11:38:41 ON 29 MAY 2002

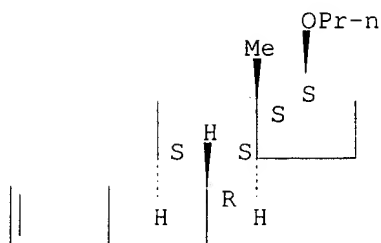
L56 1 S L53

FILE 'REGISTRY' ENTERED AT 11:38:55 ON 29 MAY 2002

=> d ide can tot l53

L53 ANSWER 1 OF 8 REGISTRY COPYRIGHT 2002 ACS  
RN 319427-04-8 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 17-propoxy-, (17.beta.)- (9CI) (CA INDEX  
NAME)  
FS STEREOSEARCH  
MF C21 H30 O2  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



HO

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:85991

REFERENCE 2: 134:101056

L53 ANSWER 2 OF 8 REGISTRY COPYRIGHT 2002 ACS

RN 126003-44-9 REGISTRY

CN Estra-1,3,5(10)-trien-3-ol, 17-(2-propynyloxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

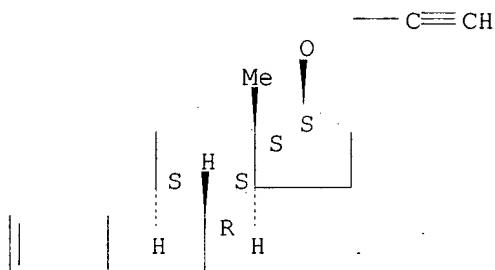
FS STEREOSEARCH

MF C21 H26 O2

SR CA

LC STN Files: BEILSTEIN\*, CA, CAPLUS, CASREACT  
 (\*File contains numerically searchable property data)

Absolute stereochemistry.



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\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 117:8261

REFERENCE 2: 112:158724

L53 ANSWER 3 OF 8 REGISTRY COPYRIGHT 2002 ACS

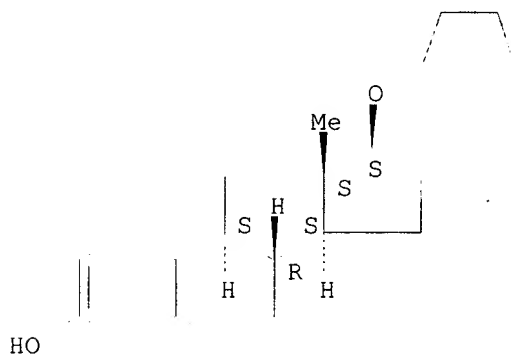
RN 85391-72-6 REGISTRY

CN Estra-1,3,5(10)-trien-3-ol, 17-(cyclopentyloxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

FS STEREOSEARCH

MF C23 H32 O2  
 SR Commission of European Communities  
 LC STN Files: CA, CAPLUS, CHEMLIST  
 Other Sources: EINECS\*\*  
 (\*\*Enter CHEMLIST File for up-to-date regulatory information)

Absolute stereochemistry.



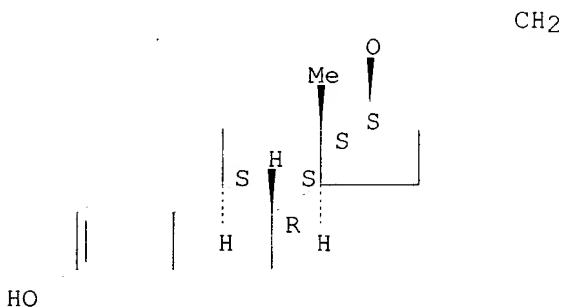
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1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 100:22887

L53 ANSWER 4 OF 8 REGISTRY COPYRIGHT 2002 ACS  
 RN 55561-41-6 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(2-propenyloxy)-, (17.beta.)- (9CI) (CA  
 INDEX NAME)  
 FS STEREOSEARCH  
 MF C21 H28 O2  
 LC STN Files: CA, CAPLUS

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
 2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 86:90134

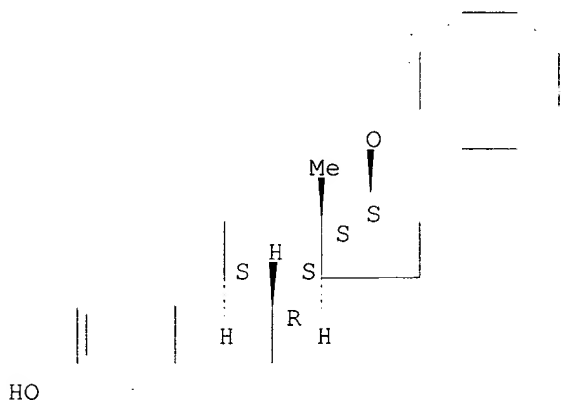
REFERENCE 2: 82:125520

L53 ANSWER 5 OF 8 REGISTRY COPYRIGHT 2002 ACS  
RN 41622-69-9 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 17-(1-cycloocten-1-yloxy)-, (17.beta.)- (9CI)  
(CA INDEX NAME)

## OTHER NAMES:

CN 17.beta.-(Cyclooct-1'-enyloxy)estra-1,3,5(10)-trien-3-ol  
FS STEREOSEARCH  
MF C26 H36 O2  
LC STN Files: CA, CAPLUS

Absolute stereochemistry.  
Double bond geometry unknown.



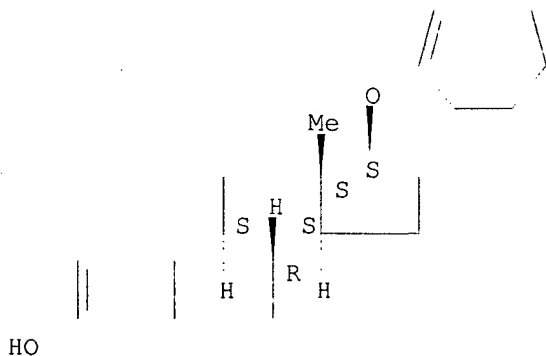
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1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 78:106316

L53 ANSWER 6 OF 8 REGISTRY COPYRIGHT 2002 ACS  
RN 41622-66-6 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 17-(1-cyclohepten-1-yloxy)-, (17.beta.)- (9CI)  
(CA INDEX NAME)  
FS STEREOSEARCH  
MF C25 H34 O2  
LC STN Files: CA, CAPLUS

Absolute stereochemistry.



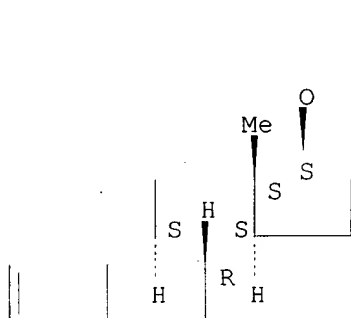
## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 78:106316

L53 ANSWER 7 OF 8 REGISTRY COPYRIGHT 2002 ACS  
RN 13885-34-2 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 17-(1-cyclohexen-1-yloxy)-, (17.beta.)- (9CI)  
(CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Estra-1,3,5(10)-trien-3-ol, 17.beta.-(1-cyclohexen-1-yloxy)- (8CI)  
FS STEREOSEARCH  
MF C24 H32 O2  
LC STN Files: BEILSTEIN\*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



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## \*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1967 TO DATE)  
3 REFERENCES IN FILE CAPLUS (1967 TO DATE)

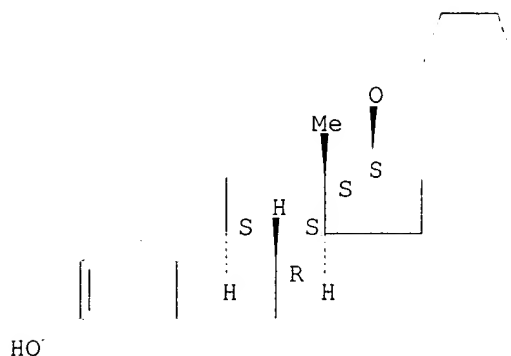
REFERENCE 1: 78:106316

REFERENCE 2: 70:68634

REFERENCE 3: 66:95293

L53 ANSWER 8 OF 8 REGISTRY COPYRIGHT 2002 ACS  
RN 13885-30-8 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 17.beta.-(1-cyclopenten-1-yloxy)- (8CI) (CA  
INDEX NAME)  
FS STEREOSEARCH  
MF C23 H30 O2  
LC STN Files: BEILSTEIN\*, CA, CAPLUS, IFICDB, IFIPAT, IFIUDB  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 70:68634

REFERENCE 2: 66:95293

=> fil uspatall

FILE 'USPATFULL' ENTERED AT 11:39:21 ON 29 MAY 2002

CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 11:39:21 ON 29 MAY 2002

CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> d bib abs hitstr 156

L56 ANSWER 1 OF 1 USPATFULL

AN 2002:61264 USPATFULL

TI Alkyl ether modified polycyclic compounds having a terminal phenol and uses for protection of cells

IN Prokai, Laszlo, Gainesville, FL, UNITED STATES  
Simpkins, James W., Fort Worth, TX, UNITED STATES

PI US 2002035100 A1 20020321

AI US 2001-893324 A1 20010627 (9)

PRAI US 2000-214077P 20000627 (60)

DT Utility

FS APPLICATION

LREP BROMBERG & SUNSTEIN LLP, 125 SUMMER STREET, BOSTON, MA, 02110-1618

CLMN Number of Claims: 46

ECL Exemplary Claim: 1

DRWN 5 Drawing Page(s)

LN.CNT 951

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and compositions are provided for achieving a cytoprotective effect by selecting a polycyclic compound with a phenol group at one end of the molecule and a carbon ring at the other such that an alkyl ether functional group in which the alkyl group has a formula  $C_{sub.n}H_{sub.2n+1}$  (where n is at least 3 and less than 20) is positioned on the carbon ring. The compound may be used to achieve a cytoprotective effect in cells and to retard the development of a degenerative condition in a subject suffering from a disease, trauma or aging.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

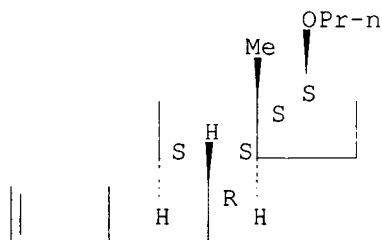
IT 319427-04-8P

(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)

RN 319427-04-8 USPATFULL

CN Estra-1,3,5(10)-trien-3-ol, 17-propoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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=&gt; fil hcaplus

FILE 'HCAPLUS' ENTERED AT 11:39:34 ON 29 MAY 2002

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PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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FILE COVERS 1907 - 29 May 2002 VOL 136 ISS 22

FILE LAST UPDATED: 27 May 2002 (20020527/ED)

This file contains CAS Registry Numbers for easy and accurate substance identification.

CAS roles have been modified effective December 16, 2001. Please check your SDI profiles to see if they need to be revised. For information on CAS roles, enter HELP ROLES at an arrow prompt or use the CAS Roles thesaurus (/RL field) in this file.

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L55 ANSWER 1 OF 10 HCAPLUS COPYRIGHT 2002 ACS

AN 2002:10439 HCAPLUS

DN 136:85991

TI Preparation of 17.beta.-alkyl ether estradiol derivatives with cytoprotective activity of cells from degeneration through disease, trauma or aging

IN Prokai, Laszlo; Simpkins, James W.

PA University of Florida Research Foundation, Inc., USA

SO PCT Int. Appl., 29 pp.

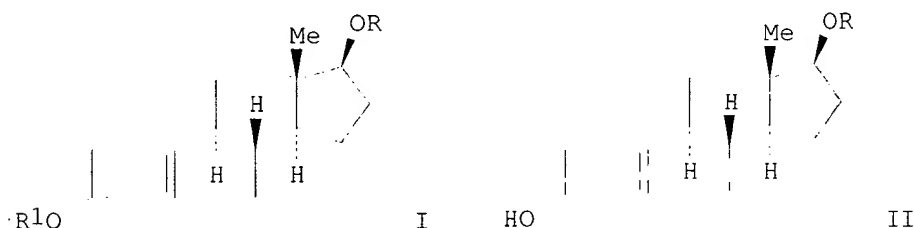
CODEN: PIXXD2

DT Patent  
 LA English  
 IC ICM C07D  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 1, 75

FAN.CNT 1

|      | PATENT NO.   | KIND | DATE     | APPLICATION NO. | DATE     |
|------|--|------|----------|-----------------|----------|
| PI   | WO 2002000619  | A2   | 20020103 | WO 2001-US41170 | 20010627 |
|      | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,<br>CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR,<br>HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT,<br>LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU,<br>SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU,<br>ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY,<br>DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF,<br>BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG |      |          |                 |          |
|      | US 2002035100  | A1   | 20020321 | US 2001-893324  | 20010627 |
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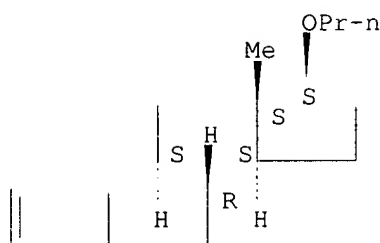
GI



- AB Cytoprotective compds. I (R = Me, Et, Pr, Bu, (CH<sub>2</sub>)<sub>5</sub>Me, or (CH<sub>2</sub>)<sub>7</sub>Me; R<sub>1</sub> = OH) were prepd. in 50-75% yields from 17.β.-estradiol. 17.β.-Estradiol and benzyl halide in K<sub>2</sub>CO<sub>3</sub> gave 93% yield of 3-benzyloxyestra-1,3,5(10)-trien-17.β.-ol which was then alkylated with the appropriate alkyl halides in DMF and NaH yielding the 3-benzyloxy protected derivs. of I which were then deprotected via catalytic hydrogenation using ammonium formate in Pd/C. Thus compds. II (R = hexyl and octyl) were prepd. in 70 and 75% resp., and were neuroprotective to a similar extent at a concn. of 10 .μM and 1 .μM. Typical compns. contain approx. 0.01-95% by wt. of active ingredient and the percentage of active ingredient will depend upon the dosage form and mode of administration; an ED of the active agent as measured in the plasma of a subject may be in the range of 5pg/mL-5000pg/mL. Cytoprotective compds. I (R = OH; R<sub>1</sub> = Bu, (CH<sub>2</sub>)<sub>7</sub>Me) were prepd. from 17.β.-estradiol and Bu or octyl bromide in K<sub>2</sub>CO<sub>3</sub> in 68 and 72% resp.
- ST estradiol hydroxy alkylated deriv prepn cytoprotective compn; neuroprotective alkyl ether steroid prepn; crystal structure butoxyestratrienol
- IT Steroids, preparation  
 RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
 (alkylation of 17.β.-OH or 3-OH; prepn. of 17.β.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Cytoprotective agents  
 (cardioprotective; prepn. of 17.β.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Nervous system

- (degeneration; prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Alkylation  
(hydroxyalkylation; prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Eye, disease  
(macula, degeneration; prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Crystal structure  
(of 17.beta.-butoxyestra-1,3,5(10)-trien-3-ol)
- IT Estrogen receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used as cytoprotective agents of cells from degeneration)
- IT Anti-Alzheimer's agents  
Anti-ischemic agents  
Bone, disease  
Drug delivery systems  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Osteoporosis  
(therapeutic agents; prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT 319427-05-9P  
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(crystal structure)
- IT 4954-12-5P 21830-24-0P 128805-68-5P 319427-03-7P  
**319427-04-8P** 319427-06-0P 319427-07-1P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT 50-28-2, 17.beta.-Estradiol, reactions 109-65-9, Butyl bromide  
111-83-1, Octyl bromide  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT 14982-15-1P 141318-37-8P 319426-98-7P 319426-99-8P 319427-00-4P  
319427-01-5P 319427-02-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT **319427-04-8P**  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- RN 319427-04-8 HCAPLUS
- CN Estra-1,3,5(10)-trien-3-ol, 17-propoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

L55 ANSWER 2 OF 10 HCAPLUS COPYRIGHT 2002 ACS  
 AN 2000:820327 HCAPLUS  
 DN 134:101056  
 TI Synthesis and Biological Evaluation of 17.beta.-Alkoxyestra-1,3,5(10)-trienes as Potential Neuroprotectants Against Oxidative Stress  
 AU Prokai, Laszlo; Oon, Su-Min; Prokai-Tatrai, Katalin; Abboud, Khalil A.; Simpkins, James W.  
 CS Center for Drug Discovery College of Pharmacy Department of Anesthesiology College of Medicine and Center for Neurobiology of Aging College of Pharmacy, University of Florida, Gainesville, FL, 32610-0497, USA  
 SO Journal of Medicinal Chemistry (2001), 44(1), 110-114  
 CODEN: JMCMAR; ISSN: 0022-2623  
 PB American Chemical Society  
 DT Journal  
 LA English  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 1, 75  
 OS CASREACT 134:101056  
 AB 17.beta.-O-Alkyl ethers (Me, Et, Pr, Bu, hexyl, and octyl) of estradiol were obtained from 3-O-benzyl-17.beta.-estradiol with sodium hydride/alkyl halide, followed by the removal of the O-benzyl protecting group via catalytic transfer hydrogenation. An increase compared to estradiol in the protection of neural (HT-22) cells against oxidative stress due to exposure of glutamate was furnished by higher (C-3 to C-8) alkyl ethers, while Me and Et ethers decreased the neuroprotective effect significantly. Lipophilic (Bu and octyl) ethers blocking the phenolic hydroxyl (3-OH) of A-ring were inactive.  
 ST alkoxyestratriene prepn neuroprotectant oxidative stress; estratriene alkoxy prepn neuroprotectant oxidative stress  
 IT Cytoprotective agents  
 (neuroprotectants; synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)  
 IT Crystal structure  
 Molecular structure  
 Oxidative stress, biological  
 (synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)  
 IT Estrogens  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)  
 IT 319427-05-9P  
 RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
 (synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-

trienes as potential neuroprotectants against oxidative stress)

IT 4954-12-5P 21830-24-0P 128805-68-5P 319427-03-7P  
319427-04-8P 319427-06-0P 319427-07-1P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT 50-28-2, 17.beta.-Estradiol, reactions  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT 14982-15-1P 141318-37-8P 319426-98-7P 319426-99-8P 319427-00-4P  
319427-01-5P 319427-02-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

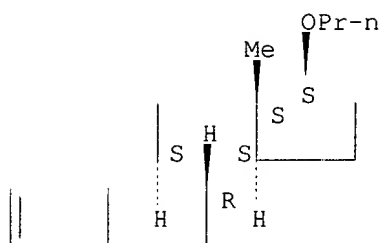
(1) Anwer, M; Synthesis 1980, P929 HCAPLUS  
(2) Behl, C; Biochem Biophys Res Commun 1995, V216, P473 HCAPLUS  
(3) Behl, C; Cell 1994, V77, P817 HCAPLUS  
(4) Behl, C; Mol Pharmacol 1997, V51, P535 HCAPLUS  
(5) Bishop, J; Mol Cell Neurosci 1994, V5, P303 HCAPLUS  
(6) Coombs, M; Steroids 1965, V6, P841 HCAPLUS  
(7) Elamin, B; J Org Chem 1979, V44, P3442 HCAPLUS  
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(10) Green, P; J Neurocytol, in press  
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(15) Gridley, K; Mol Pharmacol 1998, V54, P874 HCAPLUS  
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(18) Mook-Jung, I; Neurosci Lett 1997, V235, P101 HCAPLUS  
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(20) Paganni-Hill, A; Am J Epidemiol 1994, V140, P256  
(21) Pike, J; J Neurochem 1999, V72, P1552  
(22) Qian, X; J Steroid Biochem 1988, V29, P657 HCAPLUS  
(23) Sawada, H; J Neurosci Res 1998, V54, P707 HCAPLUS  
(24) Shearman, M; Proc Natl Acad Sci U S A 1994, V91, P470  
(25) Sheldrick, G; SHELXTL5 1998  
(26) Yankner, B; Neuron 1996, V16, P921 HCAPLUS

IT 319427-04-8P  
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)  
(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

RN 319427-04-8 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-propoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

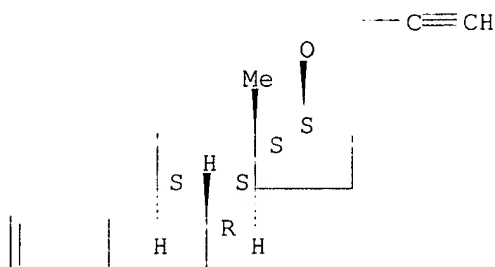


HO

- L55 ANSWER 3 OF 10 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1992:408261 HCAPLUS  
 DN 117:8261  
 TI Synthesis of o-carboranylmethyl ethers of steroids as potential target  
 substrates for boron neutron capture therapy  
 AU Schneiderova, Lenka; Strouf, Oldrich; Gruner, Bohumir; Pouzar, Vladimir;  
 Drasar, Pavel; Hampl, Richard; Kimlova, Irena  
 CS Int. Inorg. Chem., Czech. Acad. Sci., Prague, 160 00, Czech.  
 SO Collect. Czech. Chem. Commun. (1992), 57(3), 463-71  
 CODEN: CCCCAK; ISSN: 0010-0765  
 DT Journal  
 LA English  
 CC 32-3 (Steroids)  
 AB o-Carboranylmethyl ethers of steroids were synthesized by insertion of  
 steroidal 2-propynyloxy derivs. into 6,9-bis(acetonitrile)decaborane(12).  
 This reaction afforded compds. with estrane and androstane skeleton,  
 potentially useful in boron neutron capture therapy of hormone-sensitive  
 forms of cancer, i.e., 17.beta.-o-carboranylmethyl ether of estradiol (I)  
 (yield 14%) and 3.beta.- and 17.beta.-carboranylmethyl ethers of  
 androstenediol (yield 12% and 13%, resp.). Jones oxidn. afforded  
 carboranyl deriv. of androsten-17-one in 75% yield. As shown by a study  
 of the insertion reaction of 3.beta.-(2-propynyloxy)cholest-5-ene, the low  
 yields of the insertion reaction cannot be increased by changing the  
 reaction conditions. The relative binding affinity of I to estrogen  
 receptors from rat uterine and human breast tumor cytosol was 3.0 and  
 0.29% resp., of that of estradiol.  
 ST carboranylmethyl ether steroid; estrogen receptor binding  
 carboranylmethoxyestrol  
 IT Receptors  
 RL: RCT (Reactant)  
 (estrogen, binding by, of estradiol carboranylmethyl ether)  
 IT Estrogens  
 RL: RCT (Reactant)  
 (receptors, binding by, of estradiol carboranylmethyl ether)  
 IT 141887-27-6P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and binding of, to estrogen receptors)  
 IT 141870-63-5P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and oxidn. of)  
 IT 138473-74-2P 141870-64-6P 141887-25-4P 141887-26-5P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 IT 126003-29-0 126003-37-0 126003-41-6 126003-44-9  
 126003-45-0  
 RL: RCT (Reactant)  
 (reaction of, with carborane deriv.)  
 IT 17702-41-9, Decaborane(14) 28377-97-1 32124-79-1  
 RL: RCT (Reactant)

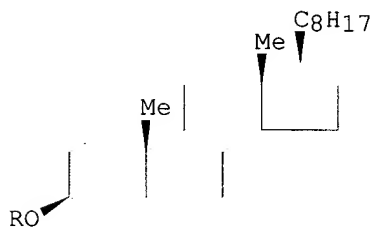
(reaction of, with hydroxy steroid)  
 IT 126003-44-9  
 RL: RCT (Reactant)  
 (reaction of, with carborane deriv.)  
 RN 126003-44-9 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(2-propynyloxy)-, (17.beta.)- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



HO

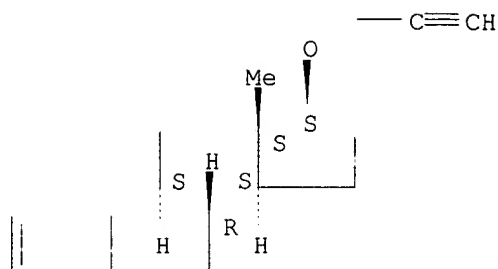
L55 ANSWER 4 OF 10 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1990:158724 HCAPLUS  
 DN 112:158724  
 TI Steroids. Part CCCXLIII. Synthesis of 2-propynyl ethers of steroid  
 alcohols  
 AU Pouzar, Vladimir; Schneiderova, Lenka; Drasar, Pavel; Strouf, Oldrich;  
 Havel, Miroslav  
 CS Inst. Org. Chem. Biochem., Slovak Acad. Sci., Prague, 166 10/6, Czech.  
 SO Collect. Czech. Chem. Commun. (1989), 54(7), 1888-902  
 CODEN: CCCCAK; ISSN: 0010-0765  
 DT Journal  
 LA English  
 CC 32-7 (Steroids)  
 OS CASREACT 112:158724  
 GI



AB Title ethers were prepd. by treating the appropriate hydroxy steroid with  
 CH.tplbond.CCH2Br under conditions of phase-transfer catalysis. Thus,  
 cholesterol (I, R = H) was treated with CH.tplbond.CCH2Br under various  
 phase-transfer conditions to give ether I (R = CH2C.tplbond.CH).  
 ST propynyl ether steroid alc  
 IT Etherification  
 (of hydroxy steroids with propargyl bromide under phase-transfer  
 conditions)  
 IT Steroids, preparation  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (propynyloxy, prepn. of, from propargyl bromide under phase-transfer

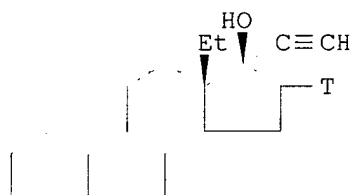
conditions)  
 IT 126003-46-1  
 RL: RCT (Reactant)  
 (Oppenauer oxidn. of)  
 IT 105644-82-4  
 RL: RCT (Reactant)  
 (detosylation-epimerization of)  
 IT 107-30-2  
 RL: RCT (Reactant)  
 (etherification by, of androstenediol acetate)  
 IT 106-96-7, Propargyl bromide  
 RL: RCT (Reactant)  
 (etherification by, of hydroxy steroids under phase-transfer conditions)  
 IT 1639-43-6  
 RL: RCT (Reactant)  
 (etherification of, with chloromethyl Me ether)  
 IT 53-43-0 57-88-5, Cholesterol, reactions 145-13-1 66168-96-5  
 88128-34-1  
 RL: RCT (Reactant)  
 (etherification of, with propargyl bromide under phase-transfer conditions)  
 IT 58-22-0  
 RL: RCT (Reactant)  
 (etherification of,, with propargyl bromide under phase-transfer conditions)  
 IT 126003-45-0P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and Oppenauer oxidn. of)  
 IT 126003-31-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and deacetylation of)  
 IT 126003-33-6P 126003-36-9P 126003-39-2P 126003-43-8P 126003-47-2P  
 126024-80-4P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and deblocking of)  
 IT 41781-86-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and etherification of, with propargyl bromide)  
 IT 5419-51-2P 126003-32-5P 126003-38-1P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and etherification of, with propargyl bromide under phase-transfer conditions)  
 IT 4975-52-4P 18000-76-5P 126003-29-0P 126003-30-3P 126003-34-7P  
 126003-35-8P 126003-37-0P 126003-40-5P 126003-41-6P 126003-42-7P  
**126003-44-9P** 126003-48-3P  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 IT 110-87-2  
 RL: RCT (Reactant)  
 (O-protection by, of hydroxysteroids)  
 IT 53-16-7, reactions  
 RL: RCT (Reactant)  
 (O-protection of, with dihydropyran)  
 IT **126003-44-9P**  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)  
 RN 126003-44-9 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(2-propynyloxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

L55 ANSWER 5 OF 10 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1984:22887 HCAPLUS  
 DN 100:22887  
 TI Tritium NMR spectroscopy of steroids  
 AU Funke, Carel W.; Kasperen, Frans M.; Wallaart, Jan; Wagenaars, Gerard N.  
 CS Sci. Dev. Group, Organon, Oss, 5340 BH, Neth.  
 SO J. Labelled Compd. Radiopharm. (1983), 20(7), 843-53  
 CODEN: JLCRD4; ISSN: 0362-4803  
 DT Journal  
 LA English  
 CC 32-5 (Steroids)  
 Section cross-reference(s): 22  
 GI



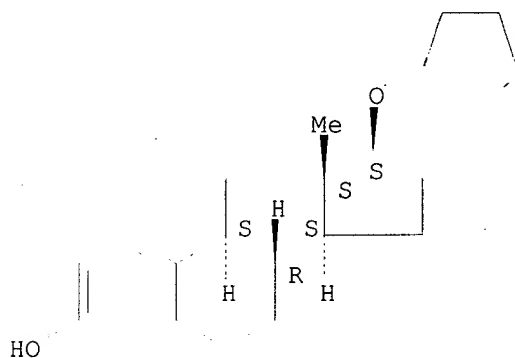
O

I

AB Seven tritiated pregnane-type steroids, e.g. I, were prepd. and their T NMR spectra were studied; these spectra gave quant. information on the T distribution in these compds.  
 ST tritium NMR steroid  
 IT Nuclear magnetic resonance  
 (of tritium, in pregnanes)  
 IT Steroids, properties  
 RL: SPN (Synthetic preparation); PREP (Preparation)  
 (hydroxy, tritium-labeled, prepn. and NMR of)  
 IT 85391-72-6  
 RL: RCT (Reactant)  
 (exchange reaction of, with tritium)  
 IT 88247-77-2P 88247-78-3P 88247-79-4P 88247-80-7P 88255-64-5P  
 88255-65-6P 88255-66-7P  
 RL: PRP (Properties); SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and NMR of)  
 IT 73991-16-9 88247-81-8  
 RL: RCT (Reactant)  
 (redn.-tritiation of)  
 IT 54024-21-4  
 RL: RCT (Reactant)  
 (tritiation and ethynylation of)  
 IT 87863-63-6 88247-82-9 88247-84-1

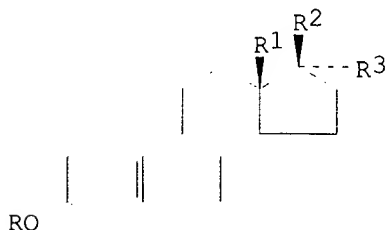
RL: RCT (Reactant)  
 (tritiation, ethynylation, and hydrolysis of)  
 IT 85391-72-6  
 RL: RCT (Reactant)  
 (exchange reaction of, with tritium)  
 RN 85391-72-6 HCAPLUS  
 CN Estradiol, 17-(cyclopentyloxy)-, (17 $\beta$ )- (9CI) (CA  
 INDEX NAME)

Absolute stereochemistry.



L55 ANSWER 6 OF 10 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1977:90134 HCAPLUS  
 DN 86:90134  
 TI Esterification of phenolic hydroxyl groups in steroids  
 IN Schwarz, Sigfrid; Weber, Gisela  
 PA E. Ger.  
 SO Ger. (East), 5 pp. Addn. to Ger. (East) 114,806.  
 CODEN: GEXXA8  
 DT Patent  
 LA German  
 IC C07C167-28  
 CC 32-3 (Steroids)  
 FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DD 120016  | Y    | 19760520 | DD 1975-184239  | 19750217 |
| GI |            |      |          |                 |          |



AB Estratrienyl sulfonates I [R = R<sub>4</sub>SO<sub>2</sub>, (R<sub>4</sub> = Me<sub>2</sub>CH, PhCH<sub>2</sub>, Me(CH<sub>2</sub>)<sub>7</sub>, 4-MeC<sub>6</sub>H<sub>4</sub>, cyclopentyl, cyclohexyl); R<sub>1</sub> = H, Me, R<sub>2</sub>R<sub>3</sub> = O, MeON; R<sub>2</sub> = HO, MeO, Me<sub>3</sub>SiO, BuCO<sub>2</sub>, EtCO<sub>2</sub>, PhCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>, CH<sub>2</sub>:CHCH<sub>2</sub>O; R<sub>2</sub> = H, HC.tplbond.C, ClC.tplbond.C, CH<sub>2</sub>:CH] (20 compds.) were prepd. in 76-97% yields by treatment of I (R = H) in H<sub>2</sub>O contg. an alkali hydroxide or an alk. earth hydroxide and a quaternary ammonium salt with R<sub>4</sub>SO<sub>2</sub>Cl. Thus, I (R = R<sub>1</sub> =

H, R2 = OH, R3 = C.tplbond.CH) in H2O-NaOH contg. (PhCH2)4N+Cl- was treated with Me2CHSO2Cl to give 80% I (R = Me2CHSO2, R1 = H, R2 = OH, R3 = C.tplbond.CH).

ST alkanesulfonate estratrienyl; sulfonation norpregnenynol; ethynylestradiol sulfonation; estradiol sulfonation; estrone sulfonation

IT 19-Norsteroids

RL: RCT (Reactant)

(3.beta.-hydroxy-17-oxygenated-1,3,5(10)-unsatd., sulfonates)

IT 28913-23-7P 28913-25-9P 29017-43-4P 29017-44-5P 29017-45-6P  
32162-69-9P 38022-64-9P 38022-65-0P 42738-04-5P 42738-09-0P  
42738-11-4P 54983-35-6P 55561-16-5P 55561-21-2P 55561-22-3P  
55561-24-5P 55561-25-6P 55561-29-0P 55561-31-4P 61872-49-9P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

IT 1939-99-7 4837-38-1 7795-95-1 10147-37-2 26394-17-2

RL: RCT (Reactant)

(reaction of, with estradienol)

IT 50-28-2, reactions 53-16-7, reactions 57-63-6 3342-64-1 3758-34-7  
4567-67-3 4954-12-5 7678-95-7 14012-72-7 26443-03-8 28416-77-5  
33526-46-4 33760-44-0 42737-82-6 55561-41-6

RL: RCT (Reactant)

(sulfonylation of)

IT 55561-41-6

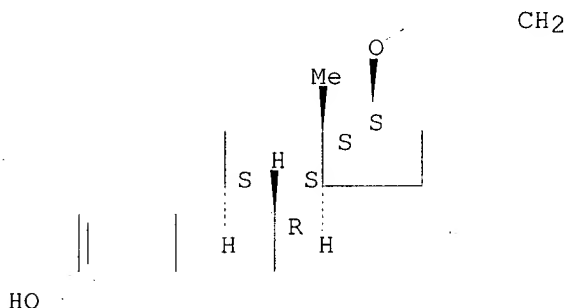
RL: RCT (Reactant)

(sulfonylation of)

RN 55561-41-6 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-(2-propenyloxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L55 ANSWER 7 OF 10 HCAPLUS COPYRIGHT 2002 ACS

AN 1975:125520 HCAPLUS

DN 82:125520

TI Steroids. 15. Sulfonyloxy derivatives of estrogens

AU Schwarz, S.; Weber, G.; Schreiber, M.

CS Wiss. Lab., VEB Jenapharm, Jena, E. Ger.

SO Pharmazie (1975), 30(1), 17-21

CODEN: PHARAT

DT Journal

LA German

CC 32-5 (Steroids)

GI For diagram(s), see printed CA Issue.

AB Estranes I (R = alkyl, cycloalkyl, CH2Ph, aminoalkyl; R1 = C.tplbond.CH, C.tplbond.CCl, CH:CH2, Et, H; R2 = OH, OSiMe3, alkoxy, acyloxy; R1R2 = O, NOH, NOSiMe3, NOAc, NOME) (66 compds.) were prepd., e.g. by treating the 3-hydroxyestranes with RSO2Cl.

ST estrane sulfonyloxy; sulfonate estrane; norpregnatrienyl alkanesulfonate; estradiol alkanesulfonate; ethynylestradiol alkanesulfonate

IT 19-Norsteroids  
RL: RCT (Reactant)  
(3-hydroxy-1,3,5(10)-unsatd., sulfonated)

IT 41781-86-6  
RL: RCT (Reactant)  
(alkylation of)

IT 57-63-6  
RL: RCT (Reactant)  
(esterification of)

IT 1689-02-7 1828-66-6 10147-37-2 10539-95-4 13360-57-1 20588-68-5  
26394-17-2 35856-62-3  
RL: RCT (Reactant)  
(esterification of 17-(trimethylsiloxy)-19-nor-17.alpha.-pregna-  
1,3,5(10)-trien-20-yn-3-ol by)

IT 10147-37-2  
RL: RCT (Reactant)  
(esterification of norpregnatrienynediol)

IT 28416-77-5  
RL: RCT (Reactant)  
(esterification of, with sulfonyl chlorides)

IT 4954-12-5P 55561-41-6P 55561-42-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and esterification of)

IT 55561-43-8P 55561-44-9P 55561-45-0P 55561-46-1P 55561-47-2P  
55561-48-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and etherification of)

IT 55561-38-1P 55561-39-2P 55561-40-5P 55561-49-4P 55561-50-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and hydrolysis of)

IT 3381-23-5P 28913-31-7P 28913-32-8P 28913-34-0P 28913-44-2P  
29017-43-4P 29017-44-5P 42738-04-5P 42738-09-0P 42738-11-4P  
52310-88-0P 52310-89-1P 52310-90-4P 54983-32-3P 54983-33-4P  
55561-09-6P 55561-10-9P 55561-11-0P 55561-12-1P 55561-13-2P  
55561-14-3P 55561-16-5P 55612-89-0P 55786-15-7P 55786-17-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and redn. of)

IT 4236-42-4P 28913-23-7P 28913-35-1P 28913-36-2P 54983-34-5P  
54983-35-6P 54983-36-7P 54983-37-8P 54983-38-9P 55561-15-4P  
55561-17-6P 55561-18-7P 55561-19-8P 55561-20-1P 55561-21-2P  
55561-23-4P 55561-24-5P 55561-25-6P 55561-26-7P 55561-27-8P  
55561-28-9P 55561-29-0P 55561-30-3P 55561-31-4P 55561-32-5P  
55561-33-6P 55561-34-7P 55561-35-8P 55561-36-9P 55561-37-0P  
55561-51-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

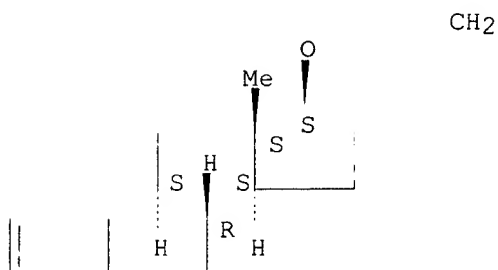
IT 55561-22-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn., esterification, and etherification of)

IT 55561-41-6P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and esterification of)

RN 55561-41-6 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-(2-propenyloxy)-, (17.beta.)- (9CI) (CA  
INDEX NAME)

Absolute stereochemistry.



HO

L55 ANSWER 8 OF 10 HCAPLUS COPYRIGHT 2002 ACS

AN 1973:106316 HCAPLUS

DN 78:106316

TI 1,3,5(10)-Estratrien-17.β.-yl enol ethers and acetals. New classes of orally and parenterally active estrogenic derivatives

AU Gardi, Rinaldo; Vitali, Romano; Falconi, Giovanni; Ercoli, Alberto

CS Warner Vistor Steroid Res. Inst., Casatenovo, Italy

SO J. Med. Chem. (1973), 16(2), 123-7

CODEN: JMCMAR

DT Journal

LA English

CC 2-5 (Hormone Pharmacology)

AB A no. of labile 17-ethers of estradiol showed uterotrophic activity greater than that of estradiol, and in some cases comparable to that of ethynylestradiol. Esp. active orally at 0.3-0.9 nmole/day in mice were cycloalkenyl ethers with 5-9-membered rings, such as 17.β.-(cyclopent-1-enyloxy)estra-1,3,5(10)-trien-3-ol propionate (I) [13885-28-4], and mixed ketals such as 17.β.-[(1-methoxycyclopentyl)oxy]estra-1,3,5(10)-trien-3-ol (II) [13885-25-1]. High and long-lasting parenteral uterotrophic activity in rats was shown after single s.c. doses of 0.05 .μmole of cycloalkenyl ethers with 8-15-membered rings such as 17.β.-(cyclooct-1-enyloxy)estra-1,3,5(10)-trien-3-ol m-chlorobenzoate [28275-58-3]. The depot activity of these compds. may result from their high lipophilicity and from slow cleavage of the ether linkage to release estradiol. The enol ethers were prepd. from the parent 17.β.-hydroxyestratrienes by acid-catalyzed exchange etherification with alkyl enol ethers or acetals of the appropriate aldehyde or ketone. The acetal and ketal derivs. were prepd. by acid-catalyzed addn. of the 17.β.-hydroxy steroid to suitable Me or Et enol ethers.

ST estradiol enol ether estrogen; uterotrophic estradiol enol ether

IT Estrogenic hormones

RL: BIOL (Biological study)

(estratrienyl acetals and enol ethers)

IT Uterus

(estratrienyl acetals and enol ethers effect on)

IT Molecular structure-biological activity relationship

(estrogenic, of estratrienyl acetals and enol ethers)

IT 53-16-7

RL: RCT (Reactant)

(acylation of)

|    |             |             |             |                    |             |
|----|-------------|-------------|-------------|--------------------|-------------|
| IT | 3000-64-4P  | 13885-25-1P | 13885-26-2P | 13885-27-3P        | 13885-28-4P |
|    | 13885-29-5P | 13885-31-9P | 13885-32-0P | <b>13885-34-2P</b> |             |
|    | 13885-35-3P | 13885-36-4P | 13945-91-0P | 13945-92-1P        | 21513-21-3P |
|    | 28151-76-0P | 28151-78-2P | 28151-79-3P | 28151-80-6P        | 28200-87-5P |
|    | 28200-89-7P | 28200-91-1P | 28200-93-3P | 28200-94-4P        | 28200-96-6P |
|    | 28200-97-7P | 28200-99-9P | 28201-00-5P | 28201-01-6P        | 28201-02-7P |
|    | 28201-03-8P | 28201-04-9P | 28201-05-0P | 28231-33-6P        | 28275-57-2P |
|    | 28275-58-3P | 28275-59-4P | 28275-62-9P | 41622-58-6P        | 41622-59-7P |

41622-60-0P 41622-64-4P 41622-65-5P **41622-66-6P**  
**41622-69-9P** 41622-83-7P 41622-84-8P 41622-92-8P  
 41622-93-9P 41622-94-0P 41622-95-1P 41622-96-2P 41622-97-3P  
 41622-98-4P 41622-99-5P 41623-00-1P 41623-01-2P 41623-02-3P  
 41623-03-4P 41623-04-5P 41623-05-6P 41623-06-7P 41623-09-0P  
 41623-10-3P 41623-11-4P 41623-12-5P 41623-16-9P 41623-20-5P  
 41623-21-6P 41680-40-4P 41787-78-4P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and estrogenic activity of)

IT 28151-74-8P 28151-75-9P 28151-77-1P 28200-88-6P 28275-51-6P  
 28275-52-7P 28275-53-8P 28275-54-9P 28275-55-0P 28275-56-1P  
 41623-22-7P 41623-27-2P 41623-29-4P 41623-30-7P 41623-35-2P  
 41623-37-4P 41623-41-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. of)

IT 502-72-7 931-57-7 41623-39-6

RL: BIOL (Biological study)  
 (reaction with estradiol esters)

IT 957-17-5

RL: BIOL (Biological study)  
 (reaction with estrones)

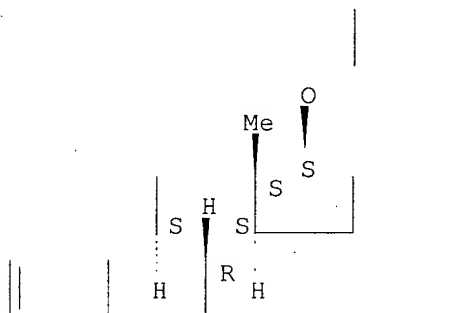
IT **13885-34-2P 41622-66-6P 41622-69-9P**

RL: SPN (Synthetic preparation); PREP (Preparation)  
 (prepn. and estrogenic activity of)

RN 13885-34-2 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-(1-cyclohexen-1-yloxy)-, (17.beta.)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.

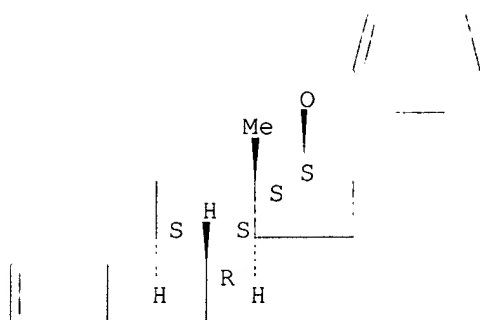


HO

RN 41622-66-6 HCAPLUS

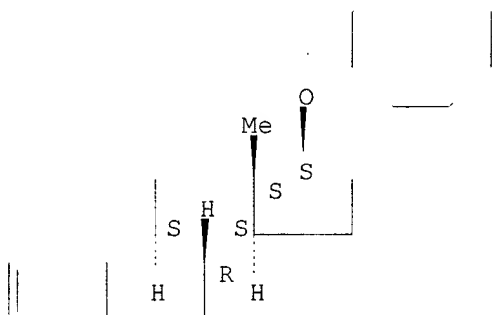
CN Estra-1,3,5(10)-trien-3-ol, 17-(1-cyclohepten-1-yloxy)-, (17.beta.)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



HO

RN 41622-69-9 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-(1-cycloocten-1-yloxy)-, (17.beta.)- (9CI)  
(CA INDEX NAME)Absolute stereochemistry.  
Double bond geometry unknown.

HO

L55 ANSWER 9 OF 10 HCAPLUS COPYRIGHT 2002 ACS

AN 1969:68634 HCAPLUS

DN 70:68634

TI 17-Ethers of estradiol

IN Ercoli, Alberto; Gardi, Rinaldo

PA Warner-Lambert Pharmaceutical Co.

SO U.S., 5 pp.

CODEN: USXXAM

DT Patent

LA English

NCL 424243000

CC 32 (Steroids)

FAN.CNT 1

|      | PATENT NO.    | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---------------|------|----------|-----------------|----------|
| PI   | US 3417183    | A    | 19681217 | US 1966-546506  | 19660502 |
|      | CH 479568     | A    | 19691015 | CH 1966-479568  | 19660601 |
|      | CH 483410     | A    | 19691231 | CH 1966-483410  | 19660601 |
|      | DK 118462     | B    | 19700824 | DK 1966-2868    | 19660603 |
|      | DK 121437     | B    | 19711018 | DK 1969-3171    | 19690612 |
| PRAI | IT 1965-12593 |      | 19650604 |                 |          |

GI For diagram(s), see printed CA Issue.

AB The title compds. (I) are prepd. by treating a 3-ester of estradiol with a

functional deriv. of a carbonyl compd. in the presence of a catalyst. Thus, a soln. of 1 g. estradiol 3-propionate (II) in 2 ml. tert-BuOH is treated with 1 ml. cyclopentanone enol methyl ether and 10 mg. p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H to give the 17-(1-methoxycyclopentyl) (A) ether of II, m. 81-3.degree. (MeOH-CH<sub>2</sub>Cl<sub>2</sub>), [.alpha.]<sub>D</sub>25 44.5.degree. (c 0.5, dioxane). Similarly is prepd. the A ether of estradiol 3-acetate (III), m. 89-91.degree., [.alpha.]<sub>D</sub>25 49.5.degree. (c 0.5%, dioxane). A soln. of 0.5 g. III in 25 ml. MeOH is refluxed 2 hrs. with 0.1N NaOH, the mixt. concd., and the residue crystd. from MeOH-CH<sub>2</sub>Cl<sub>2</sub> to give the A ether of estradiol, m. 127-9.degree., [.alpha.]<sub>D</sub>25 50.degree. (c = 0.5, dioxane). Similarly are prepd. the following I [R, R<sub>1</sub>, m.p., and [.alpha.]<sub>D</sub>25 (c 0.5, dioxane) given]: EtCO, 1-methoxycyclohexyl, -, 49.degree.; Ac, 1-methoxycyclohexyl, 79-82.degree., 51.5.degree.; H, 1-methoxycyclohexyl, 108-10.degree., 53.5.degree.; EtCO, MeOC(Me)Et, 53-7.degree., 64.degree.; H, MeOC(Me)Et, 109-13.degree., 67.5.degree.. A mixt. of 3 g. II and 5 ml. cyclopentanone diethyl acetal is heated 1 hr. at 180-200.degree., neutralized with a few drops pyridine, concd. to dryness in vacuo, and crystd. from MeOH to give the 17-(cyclopent-1-enyl) ether of II, m. 91-3.degree., [.alpha.]<sub>D</sub>25 61.5.degree. (c 0.5, dioxane). Similarly are obtained the following I [R, R<sub>1</sub>, m.p., [.alpha.]<sub>D</sub>25 (c 0.5, dioxane) given]: Ac, cyclopent-1-enyl, 126-8.degree., 65.degree.; BuCO, cyclopent-1-enyl, - (oil), 53.5.degree.; H, cyclopent-1-enyl, 73-6.degree., 66.5.degree.; EtCO, cyclohex-1-enyl, 94-6.degree., 71.degree.; Ac, cyclohex-1-enyl, 114-16.degree., 75.degree.; BuCO, cyclohex-1-enyl, - (oil), 62.5.degree.; H, cyclohex-1-enyl, 87-90.degree., 75.5.degree.. I possess valuable claudogenic and estrogenic activity, esp. suitable for oral use. It is advisable to stabilize the pharmaceutical compns. with alk. substances to prevent acid hydrolysis of the 17-ethers.

ST estradiols estrogenic; estrogenic estradiols

IT 19-Norsteroids

RL: RCT (Reactant)

(alkoxy)

IT 13885-25-1P 13885-26-2P 13885-27-3P 13885-28-4P 13885-29-5P

13885-30-8P 13885-31-9P 13885-32-0P 13885-33-1P

13885-34-2P 13885-35-3P 13885-36-4P 13885-37-5P

13945-91-0P 13945-92-1P 14258-73-2P 21513-21-3P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

IT 13885-30-8P 13885-34-2P

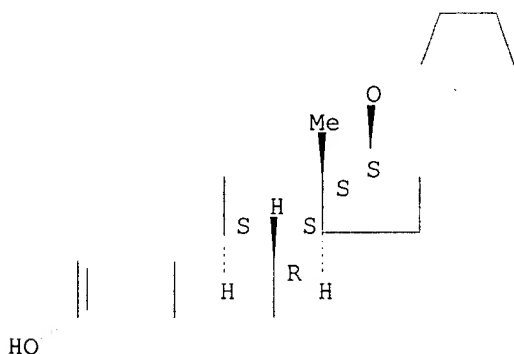
RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of)

RN 13885-30-8 HCAPLUS

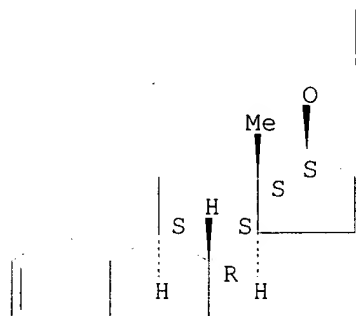
CN Estra-1,3,5(10)-trien-3-ol, 17.beta.-(1-cyclopenten-1-yloxy)- (8CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 13885-34-2 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(1-cyclohexen-1-yloxy)-, (17.β)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



HO

L55 ANSWER 10 OF 10 HCAPLUS COPYRIGHT 2002 ACS

AN 1967:95293 HCAPLUS

DN 66:95293

TI Estradiol ethers

PA Vismara, Francesco Societa per Azioni

SO Neth. Appl., 10 pp.

CODEN: NAXXAN

DT Patent

LA Dutch

IC C07C

CC 32 (Steroids)

FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE |
|------|---|------|----------|-----------------|------|
| PI   | NL 6607527  |      | 19661205 |                 |      |
| PRAI | IT  |      | 19650604 |                 |      |
| AB   | <p>Estradiol 3-propionate (I) (1 g.) in 2 cc. tert-BuOH and 1 cc. cyclopentanone enol Me ether treated about 10 min. with 10 mg. p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H yielded the 17-(1-methoxycyclopentyl) ether (II) of I, m. 81-3.degree. (CH<sub>2</sub>Cl<sub>2</sub>-MeOH), [.alpha.]<sub>D</sub><sup>25</sup> 44.5.degree. (c 0.5, dioxane). Similarly was prepd. the 17-(1-methoxycyclopentyl) ether of estradiol 3-acetate (III), m. 89-91.degree., [.alpha.]<sub>D</sub><sup>25</sup> 49.5.degree. (c 0.5, dioxane). II (0.5 g.) in 25 cc. MeOH refluxed 2 hrs. with 0.1N NaOH gave the 17-(1-methoxycyclopentyl) ether of estradiol (IV), m. 127-9.degree. [(CH<sub>2</sub>Cl)<sub>2</sub>-MeOH]. I (1 g.) in 2 cc. tert-BuOH and 1 cc. cyclohexanone enol Me ether treated with 10 mg. p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H.C<sub>5</sub>H<sub>5</sub>N (V) gave the 17-(1-methoxycyclohexyl) ether (VI) of I. Similarly was prepd. 0.95 g. 17-(1-methoxycyclohexyl) ether of III, m. 79-82.degree., [.alpha.]<sub>D</sub><sup>25</sup> 51.5.degree. (c 0.5, dioxane), from 1 g. III; its hydrolysis with 0.1N KOH gave the 17-(1-methoxycyclohexyl) ether of IV, m. 108-10.degree., [.alpha.]<sub>D</sub><sup>25</sup> 53.5.degree. (c 0.5, dioxane). I (3 g.) and 5 cc. cyclopentanone dimethyl acetal heated 1 hr. at 180-200.degree. gave the 17-(1-cyclopentenyl) ether (VII) of I, m. 91-3.degree. (MeOH), [.alpha.]<sub>D</sub><sup>25</sup> 61.5.degree. (c 0.5, dioxane). Similarly were prepd. the 17-(1-cyclopentenyl) ether of III, m. 126-8.degree., [.alpha.]<sub>D</sub><sup>25</sup> 65.degree. (c 0.5, dioxane), and the oily 17-(1-cyclopentenyl) ether of estradiol 3-valerate (VIII), [.alpha.]<sub>D</sub><sup>25</sup> 53.5.degree. (c 0.5, dioxane) VII (1.5 g.) in 50 cc. MeOH warmed 2 hrs. with 0.5 g. K<sub>2</sub>CO<sub>3</sub> in 5 cc. H<sub>2</sub>O yielded the 17-(1-cyclopentenyl) ether of IV, m. 73-6.degree., [.alpha.]<sub>D</sub><sup>25</sup> 66.5.degree. (c 0.5, dioxane). I (2 g.), 3 cc. cyclohexanone</p> |      |          |                 |      |

dimethyl acetal, 20 mg. V, and 3 cc. HCONMe<sub>2</sub> heated 1 hr. at 180-90.degree. gave the 17-(1-cyclohexenyl) ether (IX) of I, m. 94-6.degree. (CH<sub>2</sub>Cl<sub>2</sub>-MeOH), [ $\alpha$ ]<sub>D</sub><sup>25</sup> 71.degree. (c 0.5, dioxane). Similarly were prepd. the 17-(1-cyclohexenyl) ether of III, m. 114-16.degree., [ $\alpha$ ]<sub>D</sub><sup>25</sup> 75.degree. (c 0.5, dioxane), and the oily 17-(1-cyclohexenyl) ether of VIII, [ $\alpha$ ]<sub>D</sub><sup>25</sup> 62.5.degree. (c 0.5, dioxane). IX (2 g.) hydrolyzed with NaOH-MeOH gave the 17-(1-cyclohexenyl) ether of IV, m. 87-90.degree., [ $\alpha$ ]<sub>D</sub><sup>25</sup> 75.5.degree. (c 0.5, dioxane). EtMeC(OMe)<sub>2</sub> (1 g.), 30 mg. p-MeC<sub>6</sub>H<sub>4</sub>SO<sub>3</sub>H, and 5 cc. tert-BuOH with 1 g. I gave the 17-(1-methoxy-1-methylpropyl) ether of I, m. 64-8.degree., [ $\alpha$ ]<sub>D</sub><sup>25</sup> 62.degree. (c 0.5, dioxane). Similarly was prepd. the 17-(1-methoxy-1-methylpropyl) ether of III, m. 53-7.degree., [ $\alpha$ ]<sub>D</sub><sup>25</sup> 64.degree. (c 0.5, dioxane), which hydrolyzed with alkali gave the 17-(1-methoxy-1-methylpropyl) ether of IV, m. 109-13.degree., [ $\alpha$ ]<sub>D</sub><sup>25</sup> 67.5.degree. (c 0.5, dioxane).

ST ESTRADIOL CYCLOPENTYL ETHERS; CYCLOPENTYL ETHERS ESTRADIOL; ESTRADIOL CYCLOHEXYL ETHERS; CYCLOHEXYL ETHERS ESTRADIOL; ESTRADIOL CYCLOPENTENYL ETHERS; CYCLOPENTENYL ETHERS ESTRADIOL; ESTRADIOL CYCLOHEXENYL ETHERS; CYCLOHEXENYL ETHERS ESTRADIOL; ESTRADIOL PROPYL ETHERS

IT Steroids, preparation  
RL: PREP (Preparation)  
(17-alkoxy)

IT 13885-25-1P 13885-26-2P 13885-27-3P 13885-28-4P 13885-29-5P  
13885-30-8P 13885-31-9P 13885-32-0P 13885-33-1P  
13885-34-2P 13885-35-3P 13885-36-4P 13885-37-5P  
13945-91-0P 13945-92-1P 14258-73-2P

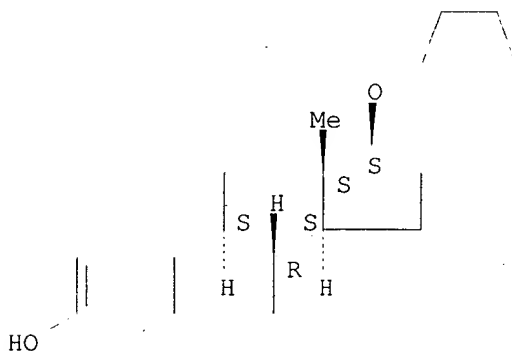
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

IT 13885-30-8P 13885-34-2P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

RN 13885-30-8 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17. $\beta$ -(1-cyclopenten-1-yloxy)- (8CI) (CA INDEX NAME)

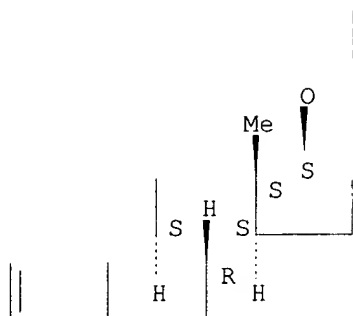
Absolute stereochemistry.



RN 13885-34-2 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-(1-cyclohexen-1-yloxy)-, (17. $\beta$ .)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



HO

=&gt; fil reg

FILE 'REGISTRY' ENTERED AT 11:45:42 ON 29 MAY 2002

USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.

PLEASE SEE "HELP USAGETERMS" FOR DETAILS.

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STRUCTURE FILE UPDATES: 27 MAY 2002 HIGHEST RN 422267-53-6

DICTIONARY FILE UPDATES: 27 MAY 2002 HIGHEST RN 422267-53-6

TSCA INFORMATION NOW CURRENT THROUGH July 7, 2001

Please note that search-term pricing does apply when  
conducting SmartSELECT searches.

Crossover limits have been increased. See HELP CROSSOVER for details.

Calculated physical property data is now available. See HELP PROPERTIES  
for more information. See STNote 27, Searching Properties in the CAS

Registry File, for complete details:

<http://www.cas.org/ONLINE/STN/STNOTES/stnotes27.pdf>

=&gt; d ide can tot 163

L63 ANSWER 1 OF 11 REGISTRY COPYRIGHT 2002 ACS

RN 319427-03-7 REGISTRY

CN Estra-1,3,5(10)-trien-3-ol, 17-ethoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

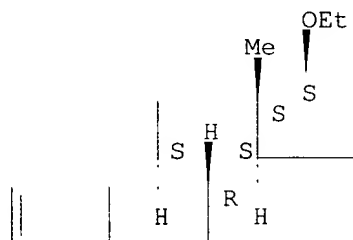
FS STEREOSEARCH

MF C20 H28 O2

SR CA

LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry.



HO

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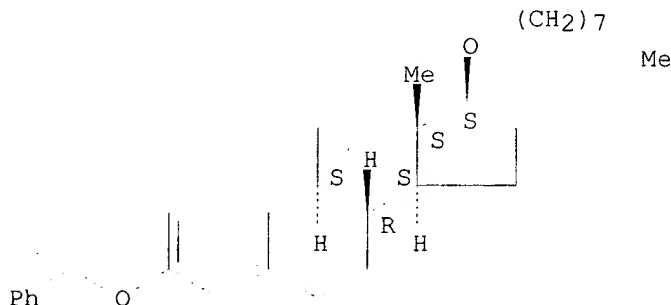
2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:85991

REFERENCE 2: 134:101056

L63 ANSWER 2 OF 11 REGISTRY COPYRIGHT 2002 ACS  
RN 319427-02-6 REGISTRY  
CN Estra-1,3,5(10)-triene, 17-(octyloxy)-3-(phenylmethoxy)-, (17.beta.)-  
(9CI) (CA INDEX NAME)  
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SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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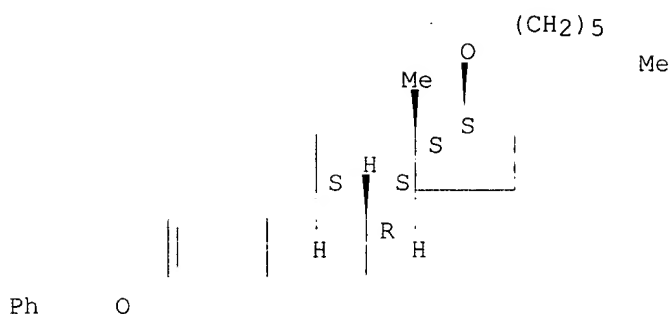
2 REFERENCES IN FILE CA (1967 TO DATE)  
2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 136:85991

REFERENCE 2: 134:101056

L63 ANSWER 3 OF 11 REGISTRY COPYRIGHT 2002 ACS  
RN 319427-01-5 REGISTRY  
CN Estra-1,3,5(10)-triene, 17-(hexyloxy)-3-(phenylmethoxy)-, (17.beta.)-  
(9CI) (CA INDEX NAME)  
FS STEREOSEARCH  
MF C31 H42 O2  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

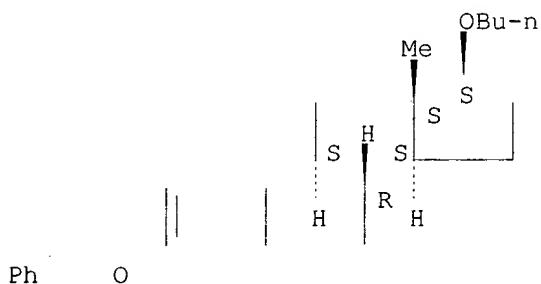
2 REFERENCES IN FILE CA (1967 TO DATE)  
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REFERENCE 1: 136:85991

REFERENCE 2: 134:101056

L63 ANSWER 4 OF 11 REGISTRY COPYRIGHT 2002 ACS  
RN **319427-00-4** REGISTRY  
CN Estra-1,3,5(10)-triene, 17-butoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
(CA INDEX NAME)  
FS STEREOSEARCH  
MF C29 H38 O2  
SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



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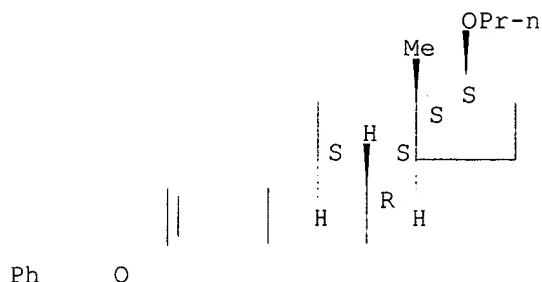
REFERENCE 1: 136:85991

REFERENCE 2: 134:101056

L63 ANSWER 5 OF 11 REGISTRY COPYRIGHT 2002 ACS  
RN **319426-99-8** REGISTRY  
CN Estra-1,3,5(10)-triene, 3-(phenylmethoxy)-17-propoxy-, (17.beta.)- (9CI)  
(CA INDEX NAME)  
FS STEREOSEARCH  
MF C28 H36 O2

SR CA  
LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

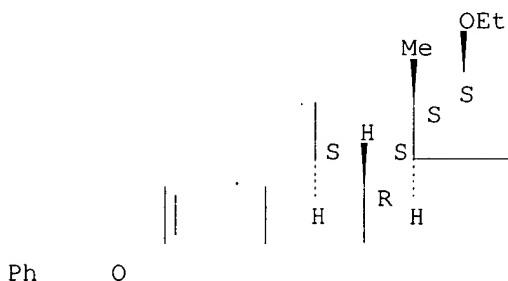
2 REFERENCES IN FILE CA (1967 TO DATE)  
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REFERENCE 1: 136:85991

REFERENCE 2: 134:101056

L63 ANSWER 6 OF 11 REGISTRY COPYRIGHT 2002 ACS  
RN 319426-98-7 REGISTRY  
CN Estra-1,3,5(10)-triene, 17-ethoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
(CA INDEX NAME)  
FS STEREOSEARCH  
MF C27 H34 O2  
SR CA  
LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

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2 REFERENCES IN FILE CAPLUS (1967 TO DATE)

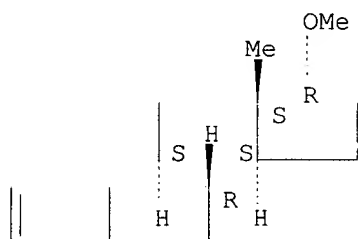
REFERENCE 1: 136:85991

REFERENCE 2: 134:101056

L63 ANSWER 7 OF 11 REGISTRY COPYRIGHT 2002 ACS  
RN 182823-27-4 REGISTRY  
CN Estra-1,3,5(10)-triene-3-ol, 17-methoxy-, (17.alpha.)- (9CI) (CA INDEX

NAME)  
 FS STEREOSEARCH  
 MF C19 H26 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



HO

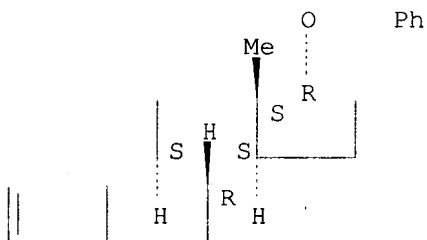
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1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:294029

L63 ANSWER 8 OF 11 REGISTRY COPYRIGHT 2002 ACS  
 RN 182624-51-7 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(phenylmethoxy)-, (17.alpha.)- (9CI) (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C25 H30 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



HO

\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

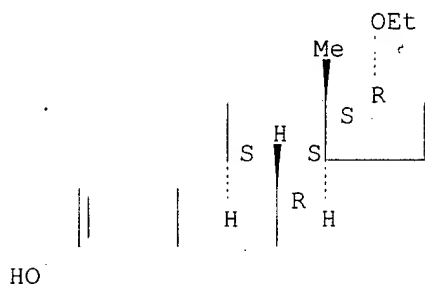
1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:294029

L63 ANSWER 9 OF 11 REGISTRY COPYRIGHT 2002 ACS  
 RN 182624-49-3 REGISTRY  
 CN Estra-1,3,5(10)-trien-3-ol, 17-ethoxy-, (17.alpha.)- (9CI) (CA INDEX

NAME)  
 FS STEREOSEARCH  
 MF C20 H28 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, USPATFULL

Absolute stereochemistry.



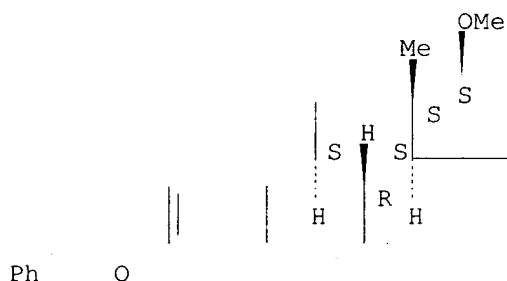
\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

1 REFERENCES IN FILE CA (1967 TO DATE)  
 1 REFERENCES IN FILE CAPLUS (1967 TO DATE)

REFERENCE 1: 125:294029

L63 ANSWER 10 OF 11 REGISTRY COPYRIGHT 2002 ACS  
 RN 141318-37-8 REGISTRY  
 CN Estra-1,3,5(10)-triene, 17-methoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
 (CA INDEX NAME)  
 FS STEREOSEARCH  
 MF C26 H32 O2  
 SR CA  
 LC STN Files: CA, CAPLUS, CASREACT, USPATFULL

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

3 REFERENCES IN FILE CA (1967 TO DATE)  
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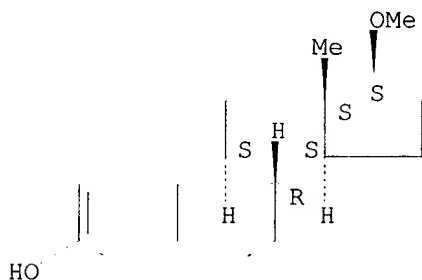
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REFERENCE 2: 134:101056

REFERENCE 3: 116:235946

L63 ANSWER 11 OF 11 REGISTRY COPYRIGHT 2002 ACS  
RN 4954-12-5 REGISTRY  
CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)  
OTHER CA INDEX NAMES:  
CN Estra-1,3,5(10)-trien-3-ol, 17.beta.-methoxy- (7CI, 8CI)  
OTHER NAMES:  
CN 17-Methoxy-1,3,5(10)-estratrien-3-ol  
CN 17.beta.-Methoxyestra-1,3,5(10)-trien-3-ol  
FS STEREOSEARCH  
MF C19 H26 O2  
LC STN Files: BEILSTEIN\*, CA, CAOLD, CAPLUS, CASREACT, TOXCENTER, USPATFULL  
(\*File contains numerically searchable property data)

Absolute stereochemistry.



\*\*PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT\*\*

16 REFERENCES IN FILE CA (1967 TO DATE)  
1 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA  
16 REFERENCES IN FILE CAPLUS (1967 TO DATE)  
3 REFERENCES IN FILE CAOLD (PRIOR TO 1967)

REFERENCE 1: 136:85991  
REFERENCE 2: 134:101056  
REFERENCE 3: 130:293190  
REFERENCE 4: 129:54482  
REFERENCE 5: 116:235946  
REFERENCE 6: 100:96847  
REFERENCE 7: 89:2201  
REFERENCE 8: 86:90134  
REFERENCE 9: 82:125520  
REFERENCE 10: 79:133109

=> d his 163-

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L63 11 S L62 NOT (ACETATE OR 17 17 DIMETHOXY)

FILE 'HCAOLD' ENTERED AT 11:45:14 ON 29 MAY 2002

L64 3 S L63

FILE 'HCAPLUS' ENTERED AT 11:45:28 ON 29 MAY 2002

L65 17 S L63

FILE 'USPATFULL, USPAT2' ENTERED AT 11:45:34 ON 29 MAY 2002

L66 4 S L63

FILE 'REGISTRY' ENTERED AT 11:45:42 ON 29 MAY 2002

=> fil uspatall

FILE 'USPATFULL' ENTERED AT 11:45:59 ON 29 MAY 2002

CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

FILE 'USPAT2' ENTERED AT 11:45:59 ON 29 MAY 2002

CA INDEXING COPYRIGHT (C) 2002 AMERICAN CHEMICAL SOCIETY (ACS)

=> d l66 bib abs hitstr tot

L66 ANSWER 1 OF 4 USPATFULL

AN 2002:61264 USPATFULL

TI Alkyl ether modified polycyclic compounds having a terminal phenol and uses for protection of cells

IN Prokai, Laszlo, Gainesville, FL, UNITED STATES  
Simpkins, James W., Fort Worth, TX, UNITED STATES

PI US 2002035100 A1 20020321

AI US 2001-893324 A1 20010627 (9)

PRAI US 2000-214077P 20000627 (60)

DT Utility

FS APPLICATION

LREP BROMBERG & SUNSTEIN LLP, 125 SUMMER STREET, BOSTON, MA, 02110-1618

CLMN Number of Claims: 46

ECL Exemplary Claim: 1

DRWN 5 Drawing Page(s)

LN.CNT 951

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Methods and compositions are provided for achieving a cytoprotective effect by selecting a polycyclic compound with a phenol group at one end of the molecule and a carbon ring at the other such that an alkyl ether functional group in which the alkyl group has a formula  $C_{sub}nH_{sub}2n+1$  (where n is at least 3 and less than 20) is positioned on the carbon ring. The compound may be used to achieve a cytoprotective effect in cells and to retard the development of a degenerative condition in a subject suffering from a disease, trauma or aging.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

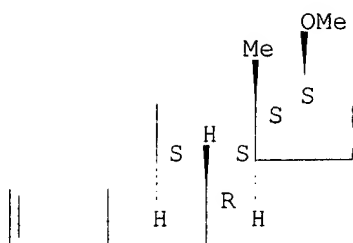
IT 4954-12-5P 319427-03-7P

(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)

RN 4954-12-5 USPATFULL

CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

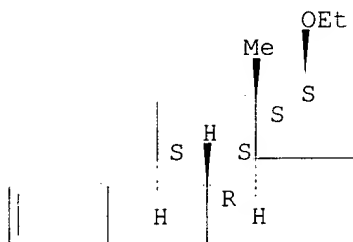


HO

RN 319427-03-7 USPATFULL

CN Estradiol, 17-ethoxy-, (17.β.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

IT 141318-37-8P 319426-98-7P 319426-99-8P

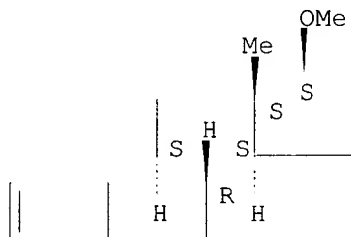
319427-00-4P 319427-01-5P 319427-02-6P

(prepn. of 17.β.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)

RN 141318-37-8 USPATFULL

CN Estradiol, 17-methoxy-3-(phenylmethoxy)-, (17.β.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



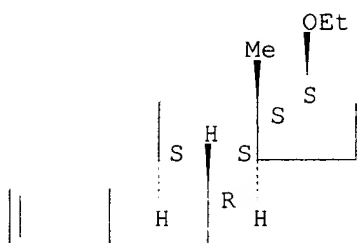
Ph

O

RN 319426-98-7 USPATFULL

CN Estradiol, 17-ethoxy-3-(phenylmethoxy)-, (17.β.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

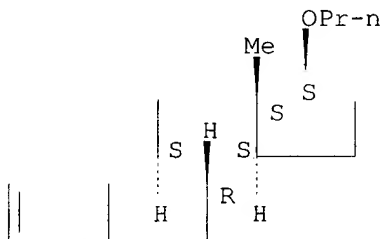


Ph O

RN 319426-99-8 USPATFULL

CN Estra-1,3,5(10)-triene, 3-(phenylmethoxy)-17-propoxy-, (17.beta.)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

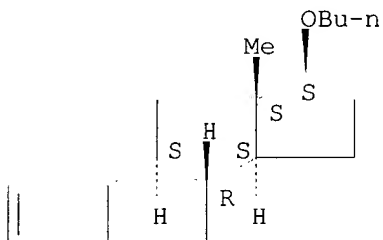


Ph O

RN 319427-00-4 USPATFULL

CN Estra-1,3,5(10)-triene, 17-butoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

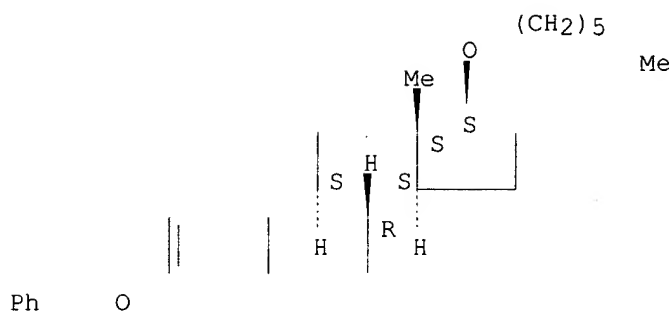


Ph O

RN 319427-01-5 USPATFULL

CN Estra-1,3,5(10)-triene, 17-(hexyloxy)-3-(phenylmethoxy)-, (17.beta.)- (9CI) (CA INDEX NAME)

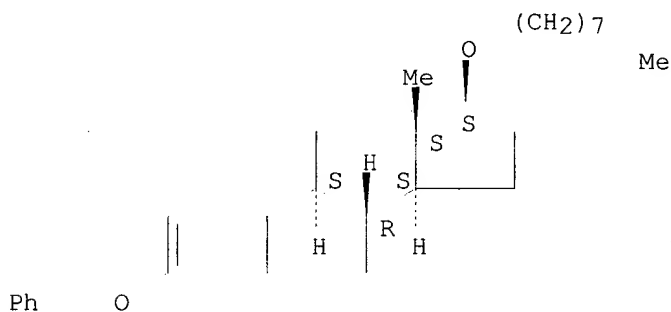
Absolute stereochemistry.



RN 319427-02-6 USPATFULL

CN Estrone-1,3,5(10)-triene, 17-(octyloxy)-3-(phenylmethoxy)-, (17.beta.)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L66 ANSWER 2 OF 4 USPATFULL

AN 1999:7375 USPATFULL

TI Steroid inhibitors of estrone sulfatase and associated pharmaceutical compositions and methods of use

IN Tanabe, Masato, Palo Alto, CA, United States

Peters, Richard H., San Jose, CA, United States

Chao, Wan-Ru, Sunnyvale, CA, United States

Shigeno, Kazuhiko, Mountain View, CA, United States

PA SRI International, Menlo Park, CA, United States (U.S. corporation)

PI US 5861388 19990119

AI US 1997-1601 19971231

RLI Division of Ser. No. US 1997-794229, filed on 29 Jan 1997, now patented,  
Pat. No. US 5763432

DT Utility

FS Granted

EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Bodio, Barbara

LREP Reed, Dianne E.Bozicevic & Reed LLP

CLMN Number of Claims: 22

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1778

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel compounds useful as inhibitors of estrone sulfatase are provided. The compounds have the structural formula (I) ##STR1## wherein X and Y, or Y and Z, form an oxathiazine dioxide ring or a dihydro-oxathiazine dioxide ring, and the other various substituents are as defined herein. Pharmaceutical compositions and methods for using the compounds of formula (I) to treat estrogen-dependent disorders are provided as well.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

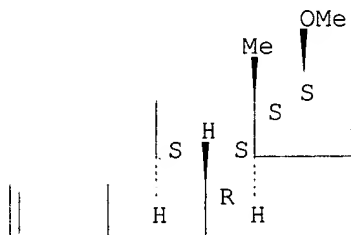
IT 4954-12-5

(prepn. of steroid inhibitors of estrone sulfatase)

RN 4954-12-5 USPTFULL

CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

L66 ANSWER 3 OF 4 USPTFULL

AN 1998:65215 USPTFULL

TI Steriod inhibitors of estrone sulfatase and associated pharmaceutical compositions and methods of use

IN Tanabe, Masato, Palo Alto, CA, United States

Peters, Richard H., San Jose, CA, United States

Chao, Wan-Ru, Sunnyvale, CA, United States

Shigeno, Kazuhiko, Mountain View, CA, United States

PA SRI International, Menlo Park, CA, United States (U.S. corporation)

PI US 5763432 19980609

AI US 1997-794229 19970129 (8)

DT Utility

FS Granted

EXNAM Primary Examiner: Dees, Jose G.; Assistant Examiner: Badio, Barbara

LREP Reed, Dianne E.Bozicevic & Reed LLP

CLMN Number of Claims: 13

ECL Exemplary Claim: 1

DRWN No Drawings

LN.CNT 1700

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB Novel compounds useful as inhibitors of estrone sulfatase are provided. The compounds have the structural formula (I) ##STR1## wherein X and Y, or Y and Z, form an oxathiazine dioxide ring or a dihydro-oxathiazine dioxide ring, and the other various substituents are as defined herein. Pharmaceutical compositions and methods for using the compounds of formula (I) to treat estrogen-dependent disorders are provided as well.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

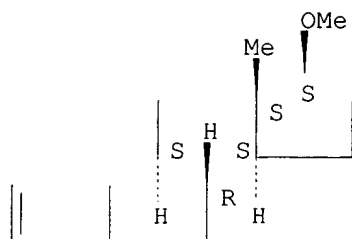
IT 4954-12-5

(prepn. of steroid inhibitors of estrone sulfatase)

RN 4954-12-5 USPTFULL

CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

L66 ANSWER 4 OF 4 USPATFULL  
 AN 96:82674 USPATFULL  
 TI Methods for neuroprotection  
 IN Simpkins, James W., Gainesville, FL, United States  
 Singh, Meharvan, Gainesville, FL, United States  
 Bishop, Jean, Jacksonville, FL, United States  
 PA University of Florida, Gainesville, FL, United States (U.S. corporation)  
 PI US 5554601 19960910  
 AI US 1994-318042 19941004 (8)  
 RLI Continuation-in-part of Ser. No. US 1993-149175, filed on 5 Nov 1993,  
 now abandoned  
 DT Utility  
 FS Granted  
 EXNAM Primary Examiner: Weddington, Kevin E.  
 LREP Bromberg & Sunstein  
 CLMN Number of Claims: 29  
 ECL Exemplary Claim: 1  
 DRWN 11 Drawing Figure(s); 10 Drawing Page(s)  
 LN.CNT 1532

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB A method is provided for conferring neuroprotection on a population of cells using estrogen compounds that have insubstantial sex activity and furthermore, a method is provided that utilizes estrogen compounds in the absence of testosterone for treating neurodegenerative diseases including Alzheimer's disease so as to retard the adverse effects of these disorders. Examples of estrogen compounds that have insubstantial sex activity includes alpha isomers of estrogen compounds such as 17.alpha. estradiol.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

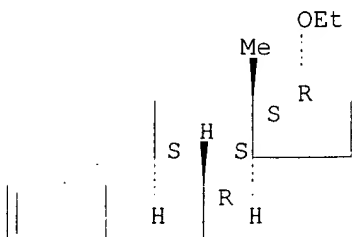
IT 182624-49-3 182624-51-7 182823-27-4

(methods for neuroprotection)

RN 182624-49-3 USPATFULL

CN Estra-1,3,5(10)-trien-3-ol, 17-ethoxy-, (17.alpha.)- (9CI) (CA INDEX NAME)

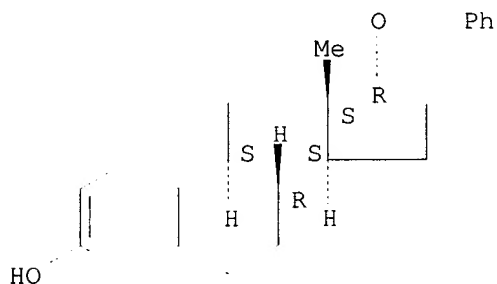
Absolute stereochemistry.



HO

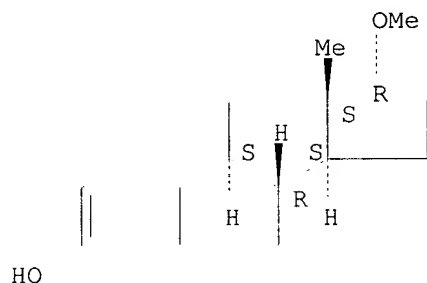
RN 182624-51-7 USPATFULL  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(phenylmethoxy)-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 182823-27-4 USPATFULL  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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 FILE LAST UPDATED: 27 May 2002 (20020527/ED)

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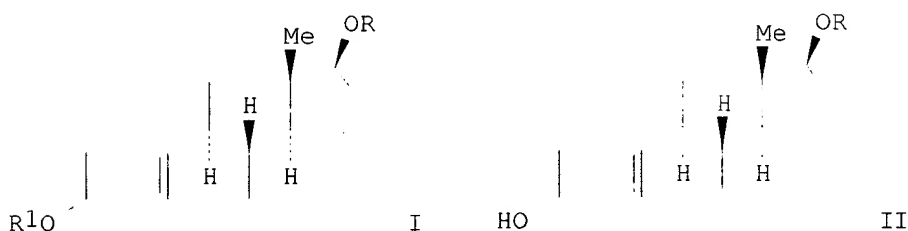
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L65 ANSWER 1 OF 17 HCAPLUS COPYRIGHT 2002 ACS  
 AN 2002:10439 HCAPLUS  
 DN 136:85991  
 TI Preparation of 17.beta.-alkyl ether estradiol derivatives with cytoprotective activity of cells from degeneration through disease, trauma or aging  
 IN Prokai, Laszlo; Simpkins, James W.  
 PA University of Florida Research Foundation, Inc., USA  
 SO PCT Int. Appl., 29 pp.  
 CODEN: PIXXD2  
 DT Patent  
 LA English  
 IC ICM C07D  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 1, 75

FAN.CNT 1

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | WO 2002000619   | A2   | 20020103 | WO 2001-US41170 | 20010627 |
|      | W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM<br>RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG |      |          |                 |          |
|      | US 2002035100   | A1   | 20020321 | US 2001-893324  | 20010627 |
| PRAI | US 2000-214077P   | P    | 20000627 |                 |          |

GI



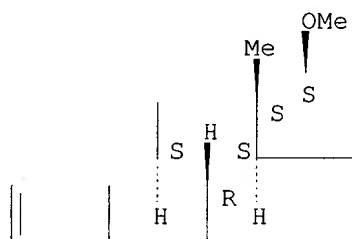
AB Cytoprotective compds. I (R = Me, Et, Pr, Bu, (CH<sub>2</sub>)<sub>5</sub>Me, or (CH<sub>2</sub>)<sub>7</sub>Me; R<sub>1</sub> = OH) were prepd. in 50-75% yields from 17.beta.-estradiol. 17.beta.-Estradiol and benzyl halide in K<sub>2</sub>CO<sub>3</sub> gave 93% yield of 3-benzyloxyestra-1,3,5(10)-trien-17.beta.-ol which was then alkylated with the appropriate alkyl halides in DMF and NaH yielding the 3-benzyloxy protected derivs. of I which were then deprotected via catalytic hydrogenation using ammonium formate in Pd/C. Thus compds. II (R = hexyl and octyl) were prepd. in 70 and 75% resp., and were neuroprotective to a similar extent at a concn. of 10 .mu.M and 1 .mu.M. Typical compns. contain approx. 0.01-95% by wt. of active ingredient and the percentage of active ingredient will depend upon the dosage form and mode of administration; an ED of the active agent as measured in the plasma of a

subject may be in the range of 5pg/mL-5000pg/mL. Cytoprotective compds. I (R = OH; R1 = Bu, (CH<sub>2</sub>)<sub>7</sub>Me) were prepd. from 17.beta.-estradiol and Bu or octyl bromide in K<sub>2</sub>CO<sub>3</sub> in 68 and 72% resp.

- ST estradiol hydroxy alkylated deriv prepn cytoprotective compn; neuroprotective alkyl ether steroid prepn; crystal structure butoxyestratrienol
- IT Steroids, preparation  
RL: PAC (Pharmacological activity); PRP (Properties); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)  
(alkylation of 17.beta.-OH or 3-OH; prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Cytoprotective agents  
(cardioprotective; prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Nervous system  
(degeneration; prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Alkylation  
(hydroxyalkylation; prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Eye, disease  
(macula, degeneration; prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Crystal structure  
(of 17.beta.-butoxyestra-1,3,5(10)-trien-3-ol)
- IT Estrogen receptors  
RL: BSU (Biological study, unclassified); BIOL (Biological study)  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used as cytoprotective agents of cells from degeneration)
- IT Anti-Alzheimer's agents  
Anti-ischemic agents  
Bone, disease  
Drug delivery systems  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT Osteoporosis  
(therapeutic agents; prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT 319427-05-9P  
RL: PAC (Pharmacological activity); PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(crystal structure)
- IT **4954-12-5P** 21830-24-0P 128805-68-5P **319427-03-7P**  
319427-04-8P 319427-06-0P 319427-07-1P  
RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT 50-28-2, 17.beta.-Estradiol, reactions 109-65-9, Butyl bromide 111-83-1, Octyl bromide  
RL: RCT (Reactant); RACT (Reactant or reagent)  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for cytoprotective activity of cells from degeneration)
- IT 14982-15-1P **141318-37-8P** **319426-98-7P**  
**319426-99-8P** **319427-00-4P** **319427-01-5P**  
**319427-02-6P**  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)  
(prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for

cytoprotective activity of cells from degeneration)  
 IT 4954-12-5P 319427-03-7P  
 RL: PAC (Pharmacological activity); SPN (Synthetic preparation); THU  
 (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES  
 (Uses)  
 (prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for  
 cytoprotective activity of cells from degeneration)  
 RN 4954-12-5 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX  
 NAME)

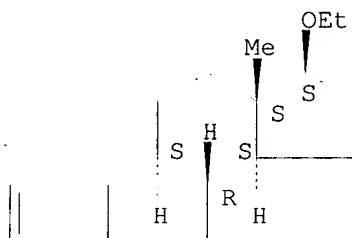
Absolute stereochemistry.



HO

RN 319427-03-7 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-ethoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

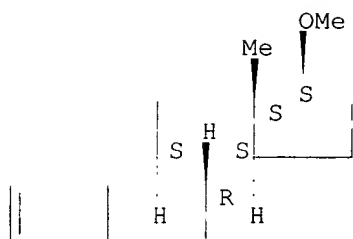
Absolute stereochemistry.



HO

IT 141318-37-8P 319426-98-7P 319426-99-8P  
 319427-00-4P 319427-01-5P 319427-02-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (prepn. of 17.beta.- or 3-alkyl ether derivs. of estradiol used for  
 cytoprotective activity of cells from degeneration)  
 RN 141318-37-8 HCAPLUS  
 CN Estra-1,3,5(10)-triene, 17-methoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.

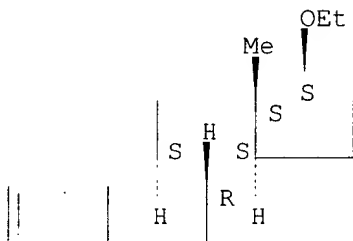


Ph O

RN 319426-98-7 HCAPLUS

CN Estra-1,3,5(10)-triene, 17-ethoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

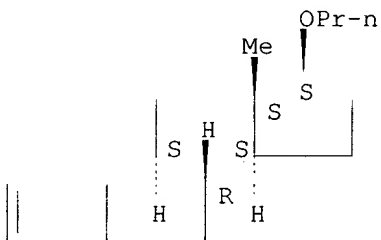


Ph O

RN 319426-99-8 HCAPLUS

CN Estra-1,3,5(10)-triene, 3-(phenylmethoxy)-17-propoxy-, (17.beta.)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

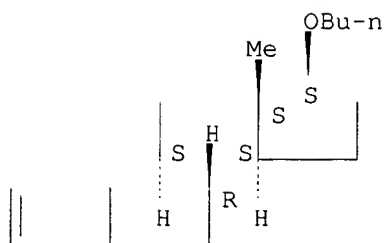


Ph O

RN 319427-00-4 HCAPLUS

CN Estra-1,3,5(10)-triene, 17-butoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.

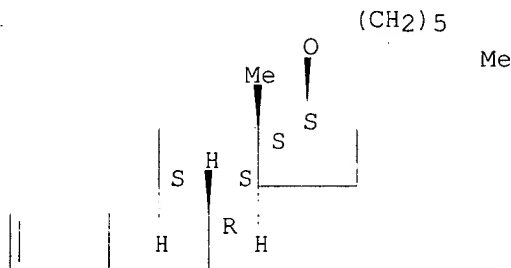


Ph O

RN 319427-01-5 HCAPLUS

CN Estra-1,3,5(10)-triene, 17-(hexyloxy)-3-(phenylmethoxy)-, (17.beta.)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.

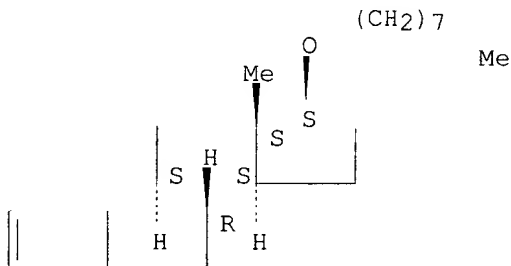


Ph O

RN 319427-02-6 HCAPLUS

CN Estra-1,3,5(10)-triene, 17-(octyloxy)-3-(phenylmethoxy)-, (17.beta.)-(9CI) (CA INDEX NAME)

Absolute stereochemistry.



Ph O

L65 ANSWER 2 OF 17 HCAPLUS COPYRIGHT 2002 ACS

AN 2000:820327 HCAPLUS

DN 134:101056

TI Synthesis and Biological Evaluation of 17.beta.-Alkoxyestra-1,3,5(10)-trienes as Potential Neuroprotectants Against Oxidative Stress

AU Prokai, Laszlo; Oon, Su-Min; Prokai-Tatrai, Katalin; Abboud, Khalil A.; Simpkins, James W.

CS Center for Drug Discovery College of Pharmacy Department of Anesthesiology College of Medicine and Center for Neurobiology of Aging College of Pharmacy, University of Florida, Gainesville, FL, 32610-0497, USA

SO Journal of Medicinal Chemistry (2001), 44(1), 110-114

CODEN: JMCMAR; ISSN: 0022-2623

PB American Chemical Society

DT Journal

LA English

CC 32-3 (Steroids)

Section cross-reference(s): 1, 75

OS CASREACT 134:101056

AB 17.beta.-O-Alkyl ethers (Me, Et, Pr, Bu, hexyl, and octyl) of estradiol were obtained from 3-O-benzyl-17.beta.-estradiol with sodium hydride/alkyl halide, followed by the removal of the O-benzyl protecting group via catalytic transfer hydrogenation. An increase compared to estradiol in the protection of neural (HT-22) cells against oxidative stress due to exposure of glutamate was furnished by higher (C-3 to C-8) alkyl ethers, while Me and Et ethers decreased the neuroprotective effect significantly. Lipophilic (Bu and octyl) ethers blocking the phenolic hydroxyl (3-OH) of A-ring were inactive.

ST alkoxyestratriene prepn neuroprotectant oxidative stress; estratriene alkoxy prepn neuroprotectant oxidative stress

IT Cytoprotective agents

(neuroprotectants; synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT Crystal structure

Molecular structure

Oxidative stress, biological

(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT Estrogens

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT 319427-05-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); PRP (Properties); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT 4954-12-5P 21830-24-0P 128805-68-5P 319427-03-7P

319427-04-8P 319427-06-0P 319427-07-1P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT 50-28-2, 17.beta.-Estradiol, reactions

RL: RCT (Reactant); RACT (Reactant or reagent)

(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

IT 14982-15-1P 141318-37-8P 319426-98-7P

319426-99-8P 319427-00-4P 319427-01-5P

319427-02-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)

(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD

RE

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IT 4954-12-5P 319427-03-7P

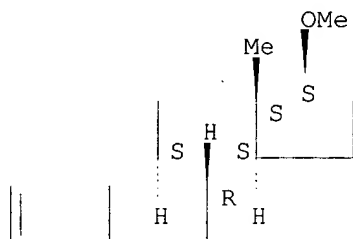
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); BIOL (Biological study); PREP (Preparation)

(synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-trienes as potential neuroprotectants against oxidative stress)

RN 4954-12-5 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

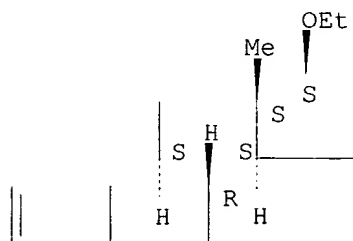


HO

RN 319427-03-7 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-ethoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

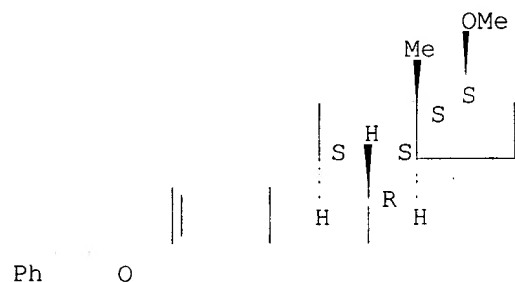
Absolute stereochemistry.



HO

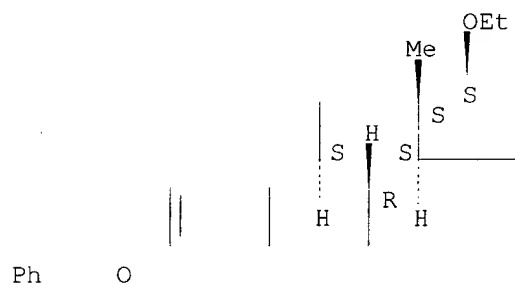
IT 141318-37-8P 319426-98-7P 319426-99-8P  
 319427-00-4P 319427-01-5P 319427-02-6P  
 RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT  
 (Reactant or reagent)  
 (synthesis and biol. evaluation of 17.beta.-alkoxyestra-1,3,5(10)-  
 trienes as potential neuroprotectants against oxidative stress)  
 RN 141318-37-8 HCAPLUS  
 CN Estra-1,3,5(10)-triene, 17-methoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



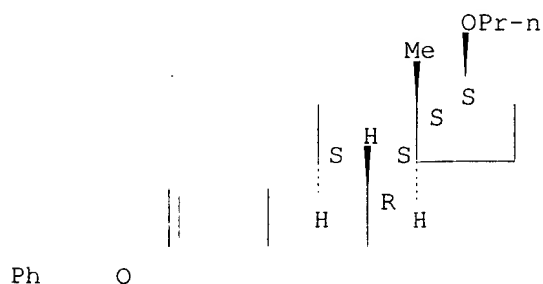
RN 319426-98-7 HCAPLUS  
 CN Estra-1,3,5(10)-triene, 17-ethoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



RN 319426-99-8 HCAPLUS  
 CN Estra-1,3,5(10)-triene, 3-(phenylmethoxy)-17-propoxy-, (17.beta.)- (9CI)  
 (CA INDEX NAME)

Absolute stereochemistry.



RN 319427-00-4 HCAPLUS  
 CN Estra-1,3,5(10)-triene, 17-butoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
 (CA INDEX NAME)

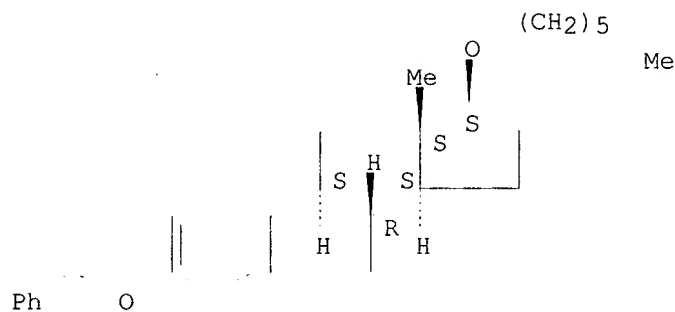
Absolute stereochemistry.



RN 319427-01-5 HCAPLUS

CN Estra-1,3,5(10)-triene, 17-(hexyloxy)-3-(phenylmethoxy)-, (17.beta.)-  
(9CI) (CA INDEX NAME)

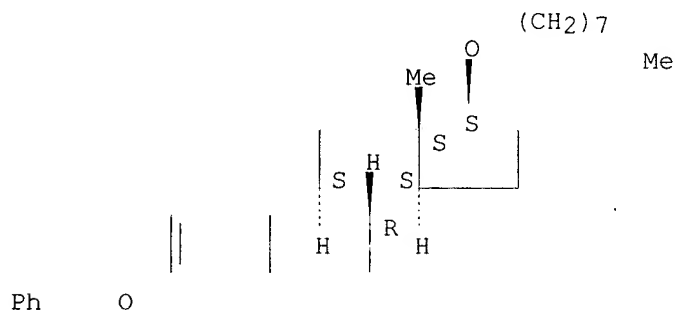
Absolute stereochemistry.



RN 319427-02-6 HCAPLUS

CN Estra-1,3,5(10)-triene, 17-(octyloxy)-3-(phenylmethoxy)-, (17.beta.)-  
(9CI) (CA INDEX NAME)

Absolute stereochemistry.



L65 ANSWER 3 OF 17 HCAPLUS COPYRIGHT 2002 ACS

AN 1999:30570 HCAPLUS

DN 130:293190

TI Human 17.beta.-hydroxysteroid dehydrogenase-ligand complexes: crystals of different space groups with various cations and combined seeding and co-crystallization

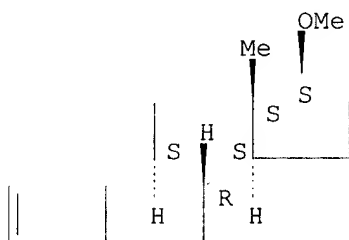
AU Zhu, D.-W.; Han, Q.; Qiu, W.; Campbell, R. L.; Xie, B.-X.; Azzi, A.; Lin, S.-X.

CS CHUL Research Center, Medical Research Council Group in Molecular

- Endocrinology, Laval University, Quebec, G1V 4G2, Can.  
 SO Journal of Crystal Growth (1999), 196(2-4), 356-364  
 CODEN: JCRGAE; ISSN: 0022-0248  
 PB Elsevier Science B.V.  
 DT Journal  
 LA English  
 CC 7-5 (Enzymes)  
 Section cross-reference(s): 75  
 AB Human estrogenic 17.beta.-hydroxysteroid dehydrogenase (17.beta.-HSD1) is responsible for the synthesis of active estrogens that stimulate the proliferation of breast cancer cells. The enzyme has been crystd. using a Mg2+/PEG (3500)/.beta.-octyl glucoside system. The space group of these crystals is C2. Here we report that cations can affect 17.beta.-HSD1 crystn. significantly. In the presence of Mn2+ instead of Mg2+, crystals have been obtained in the same space group with similar unit cell dimensions. In the presence of Li+ and Na+ instead of Mg2+, the space group has been changed to P212121. A whole data set for a crystal of 17.beta.-HSD1 complex with progesterone grown in the presence of Li+ has been collected to 1.95 .ANG. resoln. with a synchrotron source. The cell dimensions are a=41.91 .ANG., b=108.21 .ANG., c=117.00 .ANG.. The structure has been preliminarily detd. by mol. replacement, yielding important information on crystal packing in the presence of different cations. In order to further understand the structure-function relationship of 17.beta.-HSD1, enzyme complexes with several ligands have been crystd. As the steroids have very low aq. soly., we used a combined method of seeding and co-crystn. to obtain crystals of 17.beta.-HSD1 complexed with various ligands. This method provides ideal conditions for growing complex crystals, with ligands such as 20.alpha.-hydroxysteroid progesterone, testosterone and 17.beta.-methyl-estradiol-NADP+. Several complex structures have been detd. with reliable electronic d. of the bound ligands.  
 ST hydroxysteroid dehydrogenase ligand complex crystn human; crystal structure hydroxysteroid dehydrogenase ligand complex human  
 IT Cations  
 Crystal growth  
 Crystal structure  
 (crystals of human 17.beta.-hydroxysteroid dehydrogenase-ligand complexes have different space groups with various cations)  
 IT 9028-61-9, 17.beta.-Estradiol dehydrogenase  
 RL: PEP (Physical, engineering or chemical process); PRP (Properties); PROC (Process)  
 (crystals of human 17.beta.-hydroxysteroid dehydrogenase-ligand complexes have different space groups with various cations)  
 IT 53-59-8DP, Nadp, complexes with 17.beta.-hydroxysteroid dehydrogenase and 17.beta.-methylestradiol 58-22-0DP, Testosterone, complexes with 17.beta.-hydroxysteroid dehydrogenase 145-14-2DP, 20.alpha.-HydroxyProgesterone, complexes with 17.beta.-hydroxysteroid dehydrogenase 4954-12-5DP, complexes with 17.beta.-hydroxysteroid dehydrogenase and NADP 9028-61-9DP, 17.beta.-Estradiol dehydrogenase, ligand complexes  
 RL: PNU (Preparation, unclassified); PRP (Properties); PREP (Preparation)  
 (crystals of human 17.beta.-hydroxysteroid dehydrogenase-ligand complexes have different space groups with various cations)  
 RE.CNT 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD  
 RE  
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 IT 4954-12-5DP, complexes with 17.beta.-hydroxysteroid dehydrogenase and NADP  
 RL: PNU (Preparation, unclassified); PRP (Properties); PREP (Preparation) (crystals of human 17.beta.-hydroxysteroid dehydrogenase-ligand complexes have different space groups with various cations)  
 RN 4954-12-5 HCAPLUS  
 CN Estradiol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

L65 ANSWER 4 OF 17 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1998:397783 HCAPLUS  
 DN 129:54482  
 TI Preparation of steroid inhibitors of estrone sulfatase and associated pharmaceutical compositions and methods of use  
 IN Tanabe, Masato; Peters, Richard H.; Chao, Wan-ru; Shigeno, Kazuhiko  
 PA SRI International, USA  
 SO U.S., 23 pp.  
 CODEN: USXXAM  
 DT Patent  
 LA English  
 IC ICM A61K031-58  
 ICS C07J071-00  
 NCL 514176000  
 CC 32-3 (Steroids)  
 Section cross-reference(s): 1, 2

FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | US 5763432 | A    | 19980609 | US 1997-794229  | 19970129 |
|    | US 5861388 | A    | 19990119 | US 1997-1601    | 19971231 |

WO 9832763 A1 19980730 WO 1998-US1846 19980129

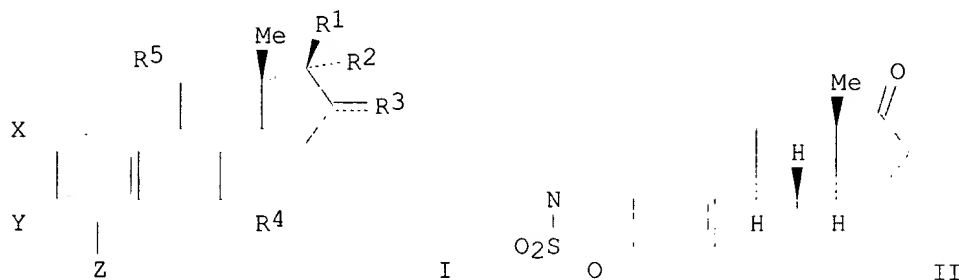
W: CA, JP, KR

RW: AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE

PRAI US 1997-794229 19970129

OS MARPAT 129:54482

GI



AB Estratriene derivs. of formula I [X and Y, or Y and Z, form an oxathiazine dioxide ring or a dihydro-oxathiazine dioxide ring; R1, R2 = H, alkyl, alkynyl, (substituted) OH; R1R2 = O, S, (substituted) CH2; R3 = H, halo, alkyl, CH2; R4 = H, alkyl; R5 = H, OH, alkyl, alkenyl, alkoxy, aryl, CH2] are prepd. as inhibitors of estrone sulfatase. Pharmaceutical compns. and methods for using I to treat estrogen-dependent disorders are provided as well. Thus, estradiol is transformed into II in 3 steps. In an estrone sulfatase inhibition assay, II showed 5-% inhibition at 9.3 nM.

ST estratriene deriv prepn estrone sulfatase inhibitor

IT 208758-20-7P 208758-22-9P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); RCT (Reactant); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); RACT (Reactant or reagent); USES (Uses)

(prepn. of steroid inhibitors of estrone sulfatase)

IT 208758-16-1P 208758-17-2P 208758-21-8P 208758-23-0P 208758-25-2P  
208758-33-2P 208758-34-3P 208758-35-4P 208758-36-5P 208758-37-6P  
208758-38-7P 208758-39-8P 208758-41-2P 208758-43-4P 208758-48-9P  
208758-52-5P 208758-54-7P

RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)

(prepn. of steroid inhibitors of estrone sulfatase)

IT 59298-96-3, Estrone sulfatase

RL: BPR (Biological process); BSU (Biological study, unclassified); MSC (Miscellaneous); BIOL (Biological study); PROC (Process)

(prepn. of steroid inhibitors of estrone sulfatase)

IT 50-28-2, Estradiol, reactions 53-16-7, Estrone, reactions 57-63-6,  
17.alpha.-Ethinylestradiol 1530-32-1, Ethyltriphenylphosphonium bromide  
1779-51-7, Butyltriphenylphosphonium bromide 4954-12-5  
6228-47-3, Propyltriphenylphosphonium bromide 7678-95-7 59077-04-2,  
19-Norpregna-1,3,5(10)-trien-3-ol

RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of steroid inhibitors of estrone sulfatase)

IT 4736-62-3P 6599-97-9P 13879-55-5P 13879-56-6P 31559-62-3P  
34111-53-0P 57711-40-7P 64215-82-3P 99898-93-8P 120574-27-8P  
120574-28-9P 123715-79-7P 137352-12-6P 206442-55-9P 208758-18-3P  
208758-19-4P 208758-24-1P 208758-26-3P 208758-27-4P 208758-28-5P  
208758-29-6P 208758-30-9P 208758-31-0P 208758-32-1P 208758-40-1P  
208758-42-3P 208758-44-5P 208758-45-6P 208758-46-7P 208758-47-8P  
208758-50-3P 208758-51-4P 208758-53-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT

(Reactant or reagent)

(prepn. of steroid inhibitors of estrone sulfatase)

IT 208758-49-0P

RL: SPN (Synthetic preparation); PREP (Preparation)

(prepn. of steroid inhibitors of estrone sulfatase)

IT 4954-12-5

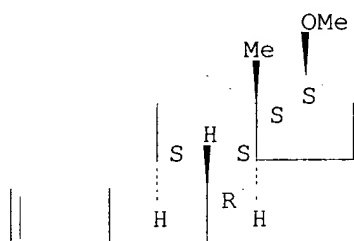
RL: RCT (Reactant); RACT (Reactant or reagent)

(prepn. of steroid inhibitors of estrone sulfatase)

RN 4954-12-5 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.β.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

L65 ANSWER 5 OF 17 HCAPLUS COPYRIGHT 2002 ACS

AN 1996:580562 HCAPLUS

DN 125:294029

TI Methods for neuroprotection

IN Simpkins, James W.; Singh, Meharvan; Bishop, Jean

PA University of Florida, USA

SO U.S., 25 pp., Cont.-in-part of U.S. Ser. No. 149,175, abandoned.

CODEN: USXXAM

DT Patent

LA English

IC ICM A61K031-56

NCL 514182000

CC 2-4 (Mammalian Hormones)

FAN.CNT 8

|      | PATENT NO.  | KIND | DATE     | APPLICATION NO. | DATE     |
|------|---|------|----------|-----------------|----------|
| PI   | US 5554601  | A    | 19960910 | US 1994-318042  | 19941004 |
|      | CA 2175603  | AA   | 19950511 | CA 1994-2175603 | 19941107 |
|      | WO 9512402  | A1   | 19950511 | WO 1994-US12782 | 19941107 |
|      | W: AU, CA, JP, KR   |      |          |                 |          |
|      | RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE    |      |          |                 |          |
|      | AU 9510901  | A1   | 19950523 | AU 1995-10901   | 19941107 |
|      | AU 699361   | B2   | 19981203 |                 |          |
|      | EP 799041   | A1   | 19971008 | EP 1995-901795  | 19941107 |
|      | R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE |      |          |                 |          |
|      | JP 11514327   | T2   | 19991207 | JP 1994-513454  | 19941107 |
|      | US 5843934  | A    | 19981201 | US 1996-648857  | 19960516 |
|      | US 5877169  | A    | 19990302 | US 1996-749703  | 19961115 |
|      | US 6319914  | B1   | 20011120 | US 1999-351492  | 19990712 |
| PRAI | US 1993-149175  | B2   | 19931105 |                 |          |
|      | US 1994-318042  | A    | 19941004 |                 |          |
|      | WO 1994-US12782   | W    | 19941107 |                 |          |
|      | US 1996-648857  | A2   | 19960516 |                 |          |
|      | US 1996-685574  | A2   | 19960724 |                 |          |
|      | US 1996-749703  | A3   | 19961115 |                 |          |
|      | US 1997-782883  | A3   | 19970110 |                 |          |

US 1998-128862 A3 19980804  
 US 1998-129209 A2 19980804  
 US 1998-179640 A3 19981027

AB A method is provided for conferring neuroprotection on a population of cells using estrogen compds. that have insubstantial sex activity and furthermore, a method is provided that utilizes estrogen compds. in the absence of testosterone for treating neurodegenerative diseases including Alzheimer's disease to retard the adverse effects of these disorders, Examples of estrogen compds. that have insubstantial sex activity includes alpha isomers of estrogen compds. such as 17.alpha.-estradiol.

ST estrogen neuroprotection

IT Nerve  
 (methods for neuroprotection)

IT Estrogens  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods for neuroprotection)

IT Molecular structure-biological activity relationship  
 (neuroprotective; methods for neuroprotection)

IT Mental disorder  
 (Alzheimer's disease, methods for neuroprotection)

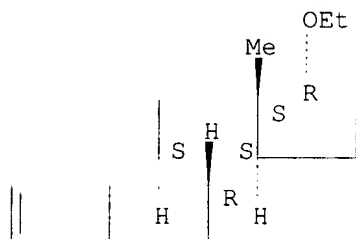
IT 53-16-7, biological studies 57-63-6, 17.alpha.-Ethinylestradiol  
 57-91-0, 17.alpha.-Estradiol 10093-54-6 15068-99-2 33602-53-8  
 65684-87-9 110114-70-0 **182624-49-3** 182624-50-6  
**182624-51-7** 182624-52-8 182624-53-9 182624-54-0  
 182624-55-1 182624-56-2 182624-57-3 182624-58-4 182624-59-5  
 182624-60-8 182624-61-9 **182823-27-4**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods for neuroprotection)

IT **182624-49-3 182624-51-7 182823-27-4**  
 RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)  
 (methods for neuroprotection)

RN 182624-49-3 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-ethoxy-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

RN 182624-51-7 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-(phenylmethoxy)-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



RN 182823-27-4 HCAPLUS  
CN Estradiol, 17-methoxy-, (17.alpha.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L65 ANSWER 6 OF 17 HCAPLUS COPYRIGHT 2002 ACS  
AN 1992:235946 HCAPLUS  
DN 116:235946  
TI Synthesis and properties of 3,17-disubstituted estrogenic steroids  
AU Tong, Z. S.; Gan, G. Z.; Li, L.; Tang, Z. M.  
CS Inst. Radiat. Med., Acad. Mil. Med. Sci., Beijing, 100850, Peop. Rep.  
China  
SO Yaoxue Xuebao (1992), 27(3), 236-40  
CODEN: YHHPAL; ISSN: 0513-4870  
DT Journal  
LA Chinese  
CC 32-3 (Steroids)  
Section cross-reference(s): 8  
GI

GI



AB Ten title radioprotective estrogens, e.g., I [R = H, Me, cyclopentyl; X = NOME, N(CH<sub>2</sub>)<sub>n</sub>CH<sub>2</sub>OH, n = 1, 2], II (R<sub>1</sub> = H, Me, CH<sub>2</sub>CH<sub>2</sub>OH) and III were prepd. I [R = cyclopentyl, X = N(CH<sub>2</sub>)<sub>n</sub>CH<sub>2</sub>OH, N = 1, 2] showed better

protective effect in mice than estradiol upon 750 rad .gamma.-irradn. with <sup>60</sup>Co. Several compds. increased 30-day survival rate by 35-80% in mice exposed to 900 rad of irradn. when administered i.p. 0.1 mg per mouse 24 h before irradn.

ST estratrienol prepn radioprotectant

IT Radioprotectants  
(estratrienols, against .gamma.-rays)

IT 141318-37-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and debenzylation of)

IT 14982-15-1P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and methylation of)

IT 2774-51-8P 4954-12-5P 6038-28-4P 27543-03-9P 94514-10-0P  
94514-11-1P 94514-13-3P 94514-15-5P 94876-43-4P 97117-16-3P  
141276-94-0P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and radioprotective activity of)

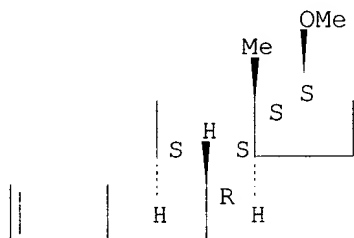
IT 141318-37-8P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and debenzylation of)

RN 141318-37-8 HCAPLUS

CN Estra-1,3,5(10)-triene, 17-methoxy-3-(phenylmethoxy)-, (17.beta.)- (9CI)  
(CA INDEX NAME)

Absolute stereochemistry.



Ph O

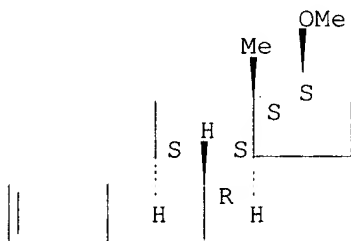
IT 4954-12-5P

RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and radioprotective activity of)

RN 4954-12-5 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

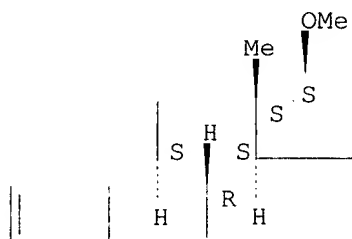
DN 100:96847  
 TI Specificity of an estrogen binding protein in the human vagina compared with that of estrogen receptors in different tissues from different species  
 AU Bergink, E. W.; Kloosterboer, H. J.; Van der Velden, W. H. M.; Van der Vies, J.; De Winter, M. S.  
 CS Sci. Dev. Group, Organon Int. B.V., Oss, Neth.  
 SO Prog. Cancer Res. Ther. (1983), 25(Steroids Endometrial Cancer), 77-84  
 CODEN: PCRTDK; ISSN: 0145-3726  
 DT Journal  
 LA English  
 CC 2-2 (Mammalian Hormones)  
 AB Estrogen-binding proteins from the myometrium, pituitary, thymus, and vagina of the rabbit; myometrium, endometrium, and vagina of the rat; and myometrium, breast tumor tissue, and MCF-7 cells of the human all displayed similar specificities with characteristics of an estrogen receptor. However, the specificity of the estrogen-binding protein in the human vagina was different from that of the human estrogen receptor; the estrogen-binding protein displayed high affinities for 17.beta.-estradiol [50-28-2], 17.alpha.-estradiol [57-91-0], and estriol [50-27-1], but a relatively low affinity for stilbestrol [56-53-1]. Structural requirements of estrogens for binding to the estrogen receptor in the rabbit myometrium were detd. and discussed.  
 ST estrogen binding protein vagina; receptor estrogen structure activity  
 IT Receptors  
 RL: BIOL (Biological study)  
 (estrogen binding by, in human and lab. animal, structure in relation to)  
 IT Neoplasm, composition  
 (estrogen receptor of, of mammary gland of human, specificity of)  
 IT Pituitary gland  
 Thymus gland  
 (estrogen receptor of, specificity of)  
 IT Vagina  
 (estrogen-binding protein of, of human and lab. animal, specificity of)  
 IT Estrogens  
 RL: PROC (Process)  
 (receptor binding of, in human and lab. animal, structure in relation to)  
 IT Molecular structure-biological activity relationship  
 (estrogen receptor-binding, of estrogens, in human and lab. animal)  
 IT Proteins  
 RL: BIOL (Biological study)  
 (estrogen-binding, of vagina, of human, specificity of)  
 IT Uterus, composition  
 (myometrium, estrogen receptor of, of human and lab. animal)  
 IT Mammary gland  
 (neoplasm, estrogen receptor of, of human, specificity of)  
 IT 50-27-1 50-28-2, biological studies 52-76-6 52-77-7 53-63-4  
 56-53-1 57-63-6 57-91-0 72-33-3 302-76-1 362-05-0 570-30-9  
 1035-77-4 1162-60-3 1229-24-9 1231-93-2 1464-61-5 1818-12-8  
 2529-54-6 2529-64-8 3398-11-6 3597-38-4 3704-15-2  
 4954-12-5 5444-22-4 6544-69-0 10448-97-2 10540-29-1  
 13570-81-5 13655-95-3 23637-93-6 34816-55-2 54502-78-2  
 54567-02-1 58212-59-2 58212-69-4 59077-04-2 66463-44-3  
 88899-71-2 88899-72-3 88899-73-4 88899-74-5 88899-75-6  
 88899-76-7 88930-00-1 88930-01-2  
 RL: PROC (Process)  
 (estrogen receptor binding of, in human and lab. animals, structure in relation to)  
 IT 4954-12-5  
 RL: PROC (Process)  
 (estrogen receptor binding of, in human and lab. animals, structure in

relation to)

RN 4954-12-5 HCAPLUS

CN Estradiol, 1,3,5(10)-trien-3-ol, 17-methoxy-, (17 $\beta$ .)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



HO

L65 ANSWER 8 OF 17 HCAPLUS COPYRIGHT 2002 ACS

AN 1978:402201 HCAPLUS

DN 89:2201

TI Structural requirements for maximal inhibitory allosteric effect of estrogens and estrogen analogs on glutamate dehydrogenase

AU Pons, Michel; Michel, Françoise; Descomps, Bernard; Crastes de Paulet, André

CS Unite Rech. Biochim. Steroides, INSERM, Montpellier, Fr.

SO Eur. J. Biochem. (1978), 84(1), 257-66

CODEN: EJBCAI; ISSN: 0014-2956

DT Journal

LA English

CC 7-3 (Enzymes)

AB The inhibition of glutamate dehydrogenase by estrogens, estrogen analogs, or polyphenylethylene derivs. (apprx.100 mols., most of them having estrogenic or antiestrogenic activities) was measured. The efficiency of these compds. in inducing allosteric inhibition of the enzyme was compared and correlated to their chem. structure: an arom. ring A, a free phenolic group in the region of C-3 of the steroid nucleus, and a lipophilic substitution in the region of C-12, C-13, or C-17 were the main structural features required for max. efficiency on glutamate dehydrogenase. A tentative model for the relative orientation of the main inhibitor families is proposed. It accounts for most of the kinetic results and can be used as a tool for the selection of affinity labels directed towards the estrogen binding site of glutamate dehydrogenase.

ST glutamate dehydrogenase inhibition estrogen

IT Estrogens

RL: BIOL (Biological study)

(glutamate dehydrogenase inhibition by)

IT Kinetics, enzymic

(of inhibition, of glutamate dehydrogenase)

IT Molecular structure-biological activity relationship

(glutamate dehydrogenase-inhibiting, of estrogens and analogs)

IT 50-27-1 50-28-2, biological studies 53-16-7, biological studies

53-63-4 56-53-1 57-63-6 57-91-0 302-76-1 481-97-0 517-04-4

517-09-9 547-81-9 566-76-7 571-92-6 1035-77-4 1089-78-7

1213-46-3 1667-98-7 1743-60-8 1818-12-8 3398-11-6 3398-12-7

3434-88-6 3597-38-4 3736-22-9 4019-92-5 4245-41-4

**4954-12-5** 5189-40-2 5444-22-4 5864-38-0 5965-06-0

5976-63-6 5976-73-8 6544-69-0 10161-33-8 10218-59-4 10448-97-2

13010-22-5 13565-53-2 13864-49-8 14418-02-1 14984-42-0

14984-43-1 20796-59-2 21507-14-2 21507-16-4 21583-10-8

22831-81-8 25547-76-6 32295-36-6 33526-45-3 34816-55-2

40128-89-0 41164-28-7 53177-70-1 60973-93-5 61665-15-4  
 62013-77-8 65928-98-5 65929-00-2 66320-32-9 66422-07-9  
 66422-09-1 66422-11-5 66422-12-6 66422-14-8 66422-17-1  
 66422-18-2 66463-40-9 66463-41-0 66463-42-1 66463-43-2  
 66463-44-3 66463-45-4 66463-46-5 66463-47-6 66463-48-7  
 66463-49-8 66463-50-1 66495-43-0 66514-24-7 66514-25-8  
 66514-26-9 66514-27-0 66537-38-0

RL: BIOL (Biological study)  
 (glutamate dehydrogenase inhibition by)

IT 9029-12-3

RL: PROC (Process)  
 (inhibition of, by estrogens and analogs)

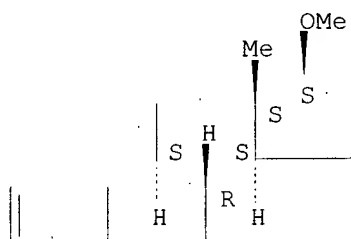
IT 4954-12-5

RL: BIOL (Biological study)  
 (glutamate dehydrogenase inhibition by)

RN 4954-12-5 HCAPLUS

CN Estr-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

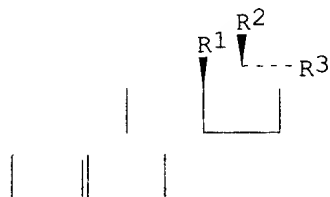
Absolute stereochemistry.



HO

L65 ANSWER 9 OF 17 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1977:90134 HCAPLUS  
 DN 86:90134  
 TI Esterification of phenolic hydroxyl groups in steroids  
 IN Schwarz, Sigfrid; Weber, Gisela  
 PA E. Ger.  
 SO Ger. (East), 5 pp. Addn. to Ger. (East) 114,806.  
 CODEN: GEXXA8  
 DT Patent  
 LA German  
 IC C07C167-28  
 CC 32-3 (Steroids)  
 FAN.CNT 1

|    | PATENT NO. | KIND | DATE     | APPLICATION NO. | DATE     |
|----|------------|------|----------|-----------------|----------|
| PI | DD 120016  | Y    | 19760520 | DD 1975-184239  | 19750217 |
| GI |            |      |          |                 |          |



RO

I

AB Estratrienyl sulfonates I [R = R<sub>4</sub>SO<sub>2</sub>, (R<sub>4</sub> = Me<sub>2</sub>CH, PhCH<sub>2</sub>, Me(CH<sub>2</sub>)<sub>7</sub>, 4-MeC<sub>6</sub>H<sub>4</sub>, cyclopentyl, cyclohexyl); R<sub>1</sub> = H, Me, R<sub>2</sub>R<sub>3</sub> = O, MeON; R<sub>2</sub> = HO, MeO, Me<sub>3</sub>SiO, BuCO<sub>2</sub>, EtCO<sub>2</sub>, PhCH<sub>2</sub>CH<sub>2</sub>CO<sub>2</sub>, CH<sub>2</sub>:CHCH<sub>2</sub>O; R<sub>2</sub> = H, HC.tplbond.C, ClC.tplbond.C, CH<sub>2</sub>:CH] (20 compds.) were prepd. in 76-97% yields by treatment of I (R = H) in H<sub>2</sub>O contg. an alkali hydroxide or an alk. earth hydroxide and a quaternary ammonium salt with R<sub>4</sub>SO<sub>2</sub>Cl. Thus, I (R = R<sub>1</sub> = H, R<sub>2</sub> = OH, R<sub>3</sub> = C.tplbond.CH) in H<sub>2</sub>O-NaOH contg. (PhCH<sub>2</sub>)<sub>4</sub>N<sup>+</sup>Cl<sup>-</sup> was treated with Me<sub>2</sub>CHSO<sub>2</sub>Cl to give 80% I (R = Me<sub>2</sub>CHSO<sub>2</sub>, R<sub>1</sub> = H, R<sub>2</sub> = OH, R<sub>3</sub> = C.tplbond.CH).

ST alkanesulfonate estratrienyl; sulfonation norpregnenynol; ethynylestradiol sulfonation; estradiol sulfonation; estrone sulfonation

IT 19-Norsteroids  
RL: RCT (Reactant)  
(3.beta.-hydroxy-17-oxygenated-1,3,5(10)-unsatd., sulfonates)

IT 28913-23-7P 28913-25-9P 29017-43-4P 29017-44-5P 29017-45-6P  
32162-69-9P 38022-64-9P 38022-65-0P 42738-04-5P 42738-09-0P  
42738-11-4P 54983-35-6P 55561-16-5P 55561-21-2P 55561-22-3P  
55561-24-5P 55561-25-6P 55561-29-0P 55561-31-4P 61872-49-9P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)

IT 1939-99-7 4837-38-1 7795-95-1 10147-37-2 26394-17-2  
RL: RCT (Reactant)  
(reaction of, with estradienol)

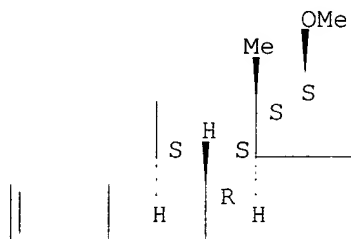
IT 50-28-2, reactions 53-16-7, reactions 57-63-6 3342-64-1 3758-34-7  
4567-67-3 4954-12-5 7678-95-7 14012-72-7 26443-03-8  
28416-77-5 33526-46-4 33760-44-0 42737-82-6 55561-41-6  
RL: RCT (Reactant)  
(sulfonylation of)

IT 4954-12-5  
RL: RCT (Reactant)  
(sulfonylation of)

RN 4954-12-5 HCAPLUS

CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

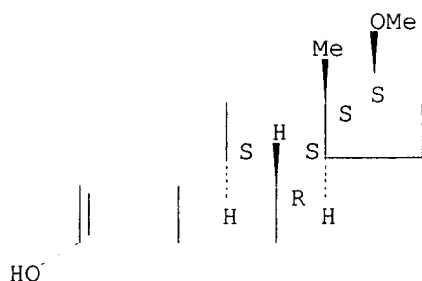


HO

L65 ANSWER 10 OF 17 HCAPLUS COPYRIGHT 2002 ACS  
AN 1975:125520 HCAPLUS  
DN 82:125520  
TI Steroids. 15. Sulfonyloxy derivatives of estrogens  
AU Schwarz, S.; Weber, G.; Schreiber, M.  
CS Wiss. Lab., VEB Jenapharm, Jena, E. Ger.  
SO Pharmazie (1975), 30(1), 17-21  
CODEN: PHARAT  
DT Journal  
LA German  
CC 32-5 (Steroids)  
GI For diagram(s), see printed CA Issue.

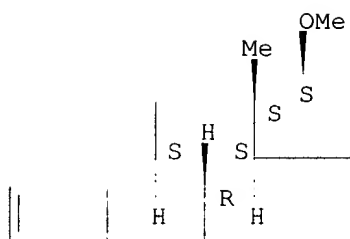
- AB Estranes I (R = alkyl, cycloalkyl, CH<sub>2</sub>Ph, aminoalkyl; R<sub>1</sub> = C.tplbond.CH, C.tplbond.CCl, CH:CH<sub>2</sub>, Et, H; R<sub>2</sub> = OH, OSiMe<sub>3</sub>, alkoxy, acyloxy; R<sub>1</sub>R<sub>2</sub> = O, NOH, NOSiMe<sub>3</sub>, NOAc, NOME) (66 compds.) were prepd., e.g. by treating the 3-hydroxyestranes with RSO<sub>2</sub>Cl.
- ST estrane sulfonyloxy; sulfonate estrane; norpregnatrienyl alkanesulfonate; estradiol alkanesulfonate; ethynylestradiol alkanesulfonate
- IT 19-Norsteroids  
RL: RCT (Reactant)  
(3-hydroxy-1,3,5(10)-unsatd., sulfonated)
- IT 41781-86-6  
RL: RCT (Reactant)  
(alkylation of)
- IT 57-63-6  
RL: RCT (Reactant)  
(esterification of)
- IT 1689-02-7 1828-66-6 10147-37-2 10539-95-4 13360-57-1 20588-68-5  
26394-17-2 35856-62-3  
RL: RCT (Reactant)  
(esterification of 17-(trimethylsiloxy)-19-nor-17.alpha.-pregna-1,3,5(10)-trien-20-yn-3-ol by)
- IT 10147-37-2  
RL: RCT (Reactant)  
(esterification of norpregnatrienynediol)
- IT 28416-77-5  
RL: RCT (Reactant)  
(esterification of, with sulfonyl chlorides)
- IT 4954-12-5P 55561-41-6P 55561-42-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and esterification of)
- IT 55561-43-8P 55561-44-9P 55561-45-0P 55561-46-1P 55561-47-2P  
55561-48-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and etherification of)
- IT 55561-38-1P 55561-39-2P 55561-40-5P 55561-49-4P 55561-50-7P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and hydrolysis of)
- IT 3381-23-5P 28913-31-7P 28913-32-8P 28913-34-0P 28913-44-2P  
29017-43-4P 29017-44-5P 42738-04-5P 42738-09-0P 42738-11-4P  
52310-88-0P 52310-89-1P 52310-90-4P 54983-32-3P 54983-33-4P  
55561-09-6P 55561-10-9P 55561-11-0P 55561-12-1P 55561-13-2P  
55561-14-3P 55561-16-5P 55612-89-0P 55786-15-7P 55786-17-9P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and redn. of)
- IT 4236-42-4P 28913-23-7P 28913-35-1P 28913-36-2P 54983-34-5P  
54983-35-6P 54983-36-7P 54983-37-8P 54983-38-9P 55561-15-4P  
55561-17-6P 55561-18-7P 55561-19-8P 55561-20-1P 55561-21-2P  
55561-23-4P 55561-24-5P 55561-25-6P 55561-26-7P 55561-27-8P  
55561-28-9P 55561-29-0P 55561-30-3P 55561-31-4P 55561-32-5P  
55561-33-6P 55561-34-7P 55561-35-8P 55561-36-9P 55561-37-0P  
55561-51-8P  
RL: SPN (Synthetic preparation); PREP (Preparation)  
(prepn. of)
- IT 55561-22-3P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn., esterification, and etherification of)
- IT 4954-12-5P  
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation)  
(prepn. and esterification of)
- RN 4954-12-5 HCAPLUS
- CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



L65 ANSWER 11 OF 17 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1973:533109 HCAPLUS  
 DN 79:133109  
 TI Comparative study of estrogen action  
 AU Raynaud, Jean P.; Bouton, Marie M.; Gallet-Bourquin, Danielle; Philibert, Daniel; Tournemine, Colette; Azadian-Boulanger, Genevieve  
 CS Cent. Rech., Roussel-Uclaf, Romainville, Fr.  
 SO Mol. Pharmacol. (1973), 9(4), 520-33  
 CODEN: MOPMA3  
 DT Journal  
 LA English  
 CC 2-3 (Hormone Pharmacology)  
 AB The tissue distribution, metab., uterine uptake, and plasma and tissue binding of 8estradiol (I) [50-28-2] and 8ethynylestradiol (II) [57-63-6] derivs. were studied in rats in vivo and in vitro, and the results were related to uterotrophic activity. Introduction of a methoxy group in position 11 of II, and esp. I, increased uterotrophic activity, whereas methylation of OH groups in positions 3 and 17 decreased it. Uterotropic activity was directly related to binding of the compds. by the 8 S uterine cytosol receptor in vivo. Activity could not be related to binding in vitro. Binding to plasma was not a prerequisite for activity but could modulate it.  
 ST estradiol deriv uterotrophic; ethynylestradiol deriv uterotrophic; uterotrophic estradiol deriv  
 IT Cytoplasm  
 (estradiol derivs. binding by, of uterus, uterotrophic activity of in relation to)  
 IT Blood plasma  
 (estradiol derivs. metab. by, uterotrophic activity in relation to)  
 IT Uterus, metabolism  
 (of estradiol derivs., uterotrophic activity in relation to)  
 IT Molecular structure-biological activity relationship  
 (uterotropic, of estradiol derivs.)  
 IT 50-28-2, biological studies 57-63-6 72-33-3 1035-77-4  
 4954-12-5 4954-14-7 7548-45-0 21507-14-2 21507-16-4  
 21507-17-5 33526-45-3 33526-46-4 33526-47-5 33526-48-6  
 33713-12-1 34816-55-2  
 RL: BIOL (Biological study)  
 (uterotropic activity of)  
 IT 4954-12-5  
 RL: BIOL (Biological study)  
 (uterotropic activity of)  
 RN 4954-12-5 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

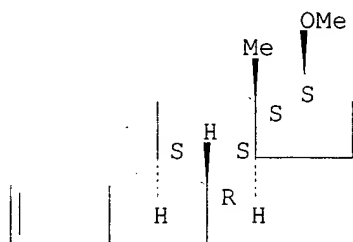


HO

L65 ANSWER 12 OF 17 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1973:427594 HCAPLUS  
 DN 79:27594  
 TI Specificity of the estrogen receptor of human uterus  
 AU Haehnel, Roland; Twaddle, Ella; Ratajczak, Thomas  
 CS Dep. Obstet. Gynaecol., King Edward Mem. Hosp., Subiaco, Aust.  
 SO J. Steroid Biochem. (1973), 4(1), 21-31  
 CODEN: JSTBBK  
 DT Journal  
 LA English  
 CC 2-3 (Hormone Pharmacology)  
 AB The estrogen receptor specificity of the human uterus was detd. from the relative abilities of various steroids to compete with 17.beta.-estradiol (I) [50-28-2] for receptor sites in the uterine cytosol fraction. Highest affinity for the receptor required a free phenolic OH group on C3 and an alc. group having the .beta.-configuration at C17, the former being particularly crit. Me groups at C1 or C4 decreased the affinity drastically, whereas the effect of a Me group at C2 was relatively slight. Addnl. O functions in ring D, addnl. substituents on ring A, and unsatn. in ring B decreased the affinity for the receptor, while the presence or absence of the angular Me group at C13 had no influence.  
 ST steroid uterus estrogen receptor  
 IT Molecular structure-biological activity relationship  
 (estrogen receptor affinity-affecting, of steroids)  
 IT Uterus  
 (estrogen receptors of, specificity of)  
 IT Receptors  
 RL: BIOL (Biological study)  
 (for estrogen, of uterus, specificity of)  
 IT 50-23-7 50-27-1 53-16-7 53-43-0 53-45-2 53-63-4 56-53-1  
 57-63-6 57-83-0, biological studies 57-91-0 58-22-0 68-96-2  
 145-13-1 434-22-0 474-86-2 481-95-8 481-96-9 481-97-0 517-09-9  
 547-81-9 566-75-6 571-20-0 793-89-5 1035-77-4 1090-04-6  
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 1852-53-5 2259-89-4 2479-91-6 2529-64-8 3232-69-7 3233-69-0  
 3434-88-6 3597-38-4 4954-12-5 5635-50-7 15093-14-8  
 15270-30-1 20431-33-8 20592-42-1 35577-54-9 35577-55-0  
 42028-17-1 42028-18-2 42028-20-6 42028-21-7  
 RL: BIOL (Biological study)  
 (estradiol binding by uterus in response to)  
 IT 50-28-2, biological studies  
 RL: BIOL (Biological study)  
 (receptors for, of uterus, specificity of)  
 IT 4954-12-5  
 RL: BIOL (Biological study)  
 (estradiol binding by uterus in response to)  
 RN 4954-12-5 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX

NAME)

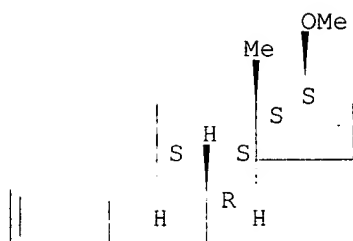
Absolute stereochemistry.



HO

L65 ANSWER 13 OF 17 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1972:561827 HCAPLUS  
 DN 77:161827  
 TI Degradation of steroids by intestinal bacteria. IV. Aromatization of ring A  
 AU Goddard, P.; Hill, M. J.  
 CS Bacterial. Dep., St. Mary's Hosp. Med. Sch., London, Engl.  
 SO Biochim. Biophys. Acta (1972), 280(2), 336-42  
 CODEN: BBACAQ  
 DT Journal  
 LA English  
 CC 10-2 (Microbial Biochemistry)  
 AB A strain of *Escherichia coli* has been shown to produce estradiol from 4-androsten-3,17-dione. From the same substrate a strain of *Clostridium paraputrificum* produced 17-methoxy-1,3,5(10)-estratriene-3-ol.  
 ST *Escherichia* metab androstenedione; *Clostridium* metab androstenedione; androstenedione bacteria intestine; steroid aromatization gut bacteria  
 IT *Escherichia coli*  
 (estradiol formation from androstenedione by)  
 IT *Clostridium paraputrificum*  
 (methoxyestratrienol formation from androstenedione by)  
 IT 63-05-8  
 RL: BIOL (Biological study)  
 (aromatization of A of, by intestinal bacteria)  
 IT 4954-12-5  
 RL: FORM (Formation, nonpreparative)  
 (formation of, from androstenedione by *Clostridium paraputrificum*)  
 IT 50-28-2, biological studies  
 RL: FORM (Formation, nonpreparative)  
 (formation of, from androstenedione by *Escherichia coli*)  
 IT 4954-12-5  
 RL: FORM (Formation, nonpreparative)  
 (formation of, from androstenedione by *Clostridium paraputrificum*)  
 RN 4954-12-5 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

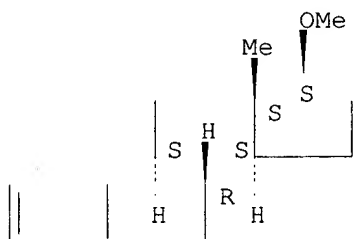
Absolute stereochemistry.



HO

L65 ANSWER 14 OF 17 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1972:11880 HCAPLUS  
 DN 76:11880  
 TI Aromatization of androst-4-ene-3,17-dione by human intestinal bacteria  
 AU Goddard, P.; Hill, M. J.  
 CS Dep. Bacteriol., St. Mary's Hosp. Med. Sch., London, Engl.  
 SO Biochem. J. (1971), 124(5), 73P  
 CODEN: BIJOAK  
 DT Journal  
 LA English  
 CC 10 (Microbial Biochemistry)  
 AB Clostridium paraputrificum grown anaerobically on broth converted androst-4-ene-3,17-dione to 17.beta.-methoxyestra-1,3,5(10)-trien-3-ol by transfer of the Me group from C-10 to the oxygen on C-17 and aromatization.  
 ST androstenedione metab Clostridium; steroid metab Clostridium; methoxyestratrienol synthesis Clostridium; estratrienol methoxy Clostridium; androgen aromatization bacterial  
 IT Clostridium paraputrificum  
 (methoxyestratrienol formation by, from androstenedione)  
 IT 63-05-8  
 RL: RCT (Reactant)  
 (aromatization of, by Clostridium paraputrificum)  
 IT 4954-12-5  
 RL: FORM (Formation, nonpreparative)  
 (formation of, from androstenedione by Clostridium paraputrificum)  
 IT 4954-12-5  
 RL: FORM (Formation, nonpreparative)  
 (formation of, from androstenedione by Clostridium paraputrificum)  
 RN 4954-12-5 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

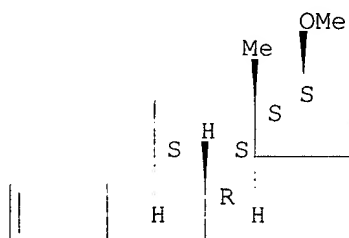


HO

L65 ANSWER 15 OF 17 HCAPLUS COPYRIGHT 2002 ACS

AN 1971:459189 HCAPLUS  
 DN 75:59189  
 TI Pharmacodynamic model for studying the mode of action of estrogens using radioactive compounds  
 AU Raynaud, Jean P.; Azadian-Boulanger, Genevieve; Bourquin, Daniele; Philibert, Daniel  
 CS Cent. Rech. Roussel-Uclaf, Romainville, FR  
 SO Symp. Progr. Tech. Nucl. Pharmacodyn. (1971), Meeting Date 1970, 39-51. Editor(s): Valette, Guillaume. Publisher: Masson, Paris, Fr. CODEN: 23IDAY  
 DT Conference  
 LA French  
 CC 4 (Hormones and Related Substances)  
 AB Radioactive steroid was injected into prepubertal rats which were then sacrificed. The increased wt. of the uterus as well as its incorporation of radioactivity was measured as a function of time, 0 to 70 hr, and anal. was made of estradiol, ethynyl estradiol, and 2 other derivs. The uterus reached a max. wt. at 30-40 hr. The radioactive steroids in the uterus peaked at 1-2 hr and by 10 hr were falling, while estrogen metabolites in the plasma were rising. A math. relation between the wt. of the uterus and the concn. of steroid and metabolites is derived.  
 ST estrogen action mode; uterus wt estrogen; plasma metabolite estrogen  
 IT Estrogenic hormones  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (metabolism of, by uterus, mol. structure in relation to)  
 IT Simulation, model  
 (of estrogens metabolism by uterus)  
 IT Uterus, metabolism  
 (of estrogens, model for)  
 IT Molecular structure-biological activity relationships  
 (uterus-binding, of estrogens)  
 IT 72-33-3 1035-77-4 **4954-12-5** 4954-14-7 7548-45-0  
 21507-16-4 21507-17-5 33526-45-3 33526-46-4 33526-47-5  
 33526-48-6 33713-12-1  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (metabolism of, by uterus)  
 IT 50-28-2, biological studies 57-63-6 21507-14-2 25918-89-2  
 RL: BIOL (Biological study)  
 (uterus binding of, estrogens effect on)  
 IT **4954-12-5**  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (metabolism of, by uterus)  
 RN 4954-12-5 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

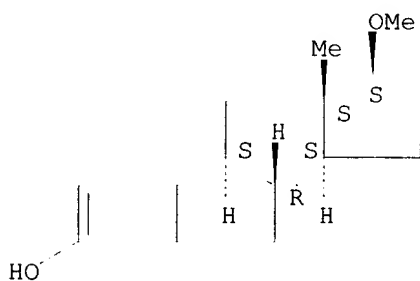
Absolute stereochemistry.



HO

DN 73:32065  
 TI Action of natural, synthetic, and semisynthetic estrogens on deciduoma formation in rat uterus  
 AU Yoshino, Akio  
 CS Sch. Med., Jikei Univ., Tokyo, Japan  
 SO Tokyo Joshi Ika Daigaku Zasshi (1969), 84(5), 562-70  
 CODEN: TJIZAF  
 DT Journal  
 LA Japanese  
 CC 4 (Hormones and Related Substances)  
 AB Estrogens (I) priming action was examd. with natural synthetic and semisynthetic I on deciduoma formation in rat uterus and metabolism of phospholipid, cholesterol, and nucleic acid in decidual tissue. Female rats, weighing about 160 g, were used at 3 weeks after ovariectomy. Estrone, estradiol, estriol, estrone sulfate, estrone Me ether, estradiol Me ether, estrone benzoate, estradiol benzoate, ethynyl-estradiol, diethylstilbestrol, and hexestrol were used. The natural I were effective primers for the deciduoma formation in rat uterus; synthetic I did not have this action. Natural I had more effect on phospholipid and cholesterol metabolism in rat uterus than synthetic I. Natural and synthetic I showed effects on nucleic acid metabolism.  
 ST estrogens deciduoma uterus; deciduoma uterus estrogens; uterus deciduoma estrogens  
 IT Nucleic acids  
 Phospholipids  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (metabolism of, by uterus, estrogens effect on)  
 IT Uterus, metabolism (of lipids and nucleic acids, estrogens effect on)  
 IT 50-27-1 50-28-2, biological studies 50-50-0 53-16-7, biological studies 56-53-1 57-63-6 481-97-0 1035-77-4 1624-62-0 2393-53-5 4954-12-5 5635-50-7  
 RL: BIOL (Biological study) (lipid and nucleic acid metabolism by uterus in response to)  
 IT 57-88-5, biological studies  
 RL: BPR (Biological process); BIOL (Biological study); PROC (Process) (metabolism of, by uterus, estrogens effect on)  
 IT 4954-12-5  
 RL: BIOL (Biological study) (lipid and nucleic acid metabolism by uterus in response to)  
 RN 4954-12-5 HCAPLUS  
 CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.

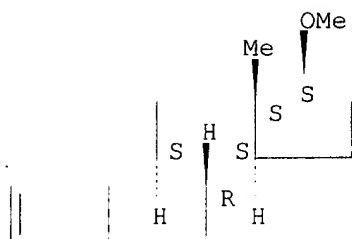


L65 ANSWER 17 OF 17 HCAPLUS COPYRIGHT 2002 ACS  
 AN 1969:477753 HCAPLUS  
 DN 71:77753  
 TI Mechanism of estrogen action in relation to carcinogenesis

AU Jensen, Elwood V.  
CS Univ. of Chicago, Chicago, Ill., USA  
SO Proc. Can. Cancer Res. Conf. (1966), Volume Date 1964, 6, 143-65  
CODEN: PCCRA4  
DT Journal  
LA English  
CC 4 (Hormones)  
AB cf. CA 57:6523d. When 3H-labeled estradiol (I) or 17.alpha.-methylestradiol (II) was given s.c. in saline to Sprague-Dawley rats, absorption was rapid and the level of radioactivity in the blood and nonresponsive tissues reached a max. in 15 min., then fell rapidly, while the uterus and vagina continued to incorporate and retain radioactivity. When I or II was given s.c. in sesame oil, the levels in liver and nonresponsive tissues paralleled that in the blood, but in the uterus, vagina, anterior pituitary, and 7,12-dimethylbenz(a)anthracene - induced mammary tumors, there was a progressive uptake and retention. With hexestrol (III), retention in the vagina and uterus was more prolonged. The affinity of the uterus for estriol (IV) was not as striking as for I, but there was some retention in the growth-responsive tissues. The uterus and vagina showed no special affinity for estrone (V). Most of the uterine radioactivity after I administration was in the myometrium. The highest concn. of radioactivity was in the lamina propria with the radioactivity decreasing from the inner to outer myometrium. I was not readily taken up and retained by epithelial cells. After the administration of 0.1 .mu.g. I, II, or IV, all the radioactivity in the uterus and vagina was in the free steroid fraction after 15 min., 2 hrs., or 6 hrs., resp.; the same was observed in the 2 hr. uteri of III-treated animals. With V, free steroid predominated in the uterus, with some water-sol. radioactivity, but the liver and blood contained radioactivity bound to the alc.-insol. fraction and in the water-sol. form. After administration of I, II, or III, only I, II, or III appeared in the uterus and vagina, while injected IV appeared in the uterus as IV with small amts. of other polar steroids. After V administration, V was present in the uterus after 15 min. but after 2 hrs. V was gone and I was present. Metabolic transformation of I, II, and III occurred in the liver, but I, II, and III evidently stimulate growth in the rat uterus without undergoing metabolic transformation. An early if not initial step in the physiol. action of estrogenic hormones is an assocn. with receptor sites present in the uterus, vagina, and anterior pituitary. Interaction does not involve covalent bonds but is strong enough in vivo to permit the uptake and retention of steroid against a concn. gradient. The initial assocn. of estrogen with receptor sites was inhibited by estrogen antagonists like U-11100 and MER-25 but not actinomycin D or puromycin.

ST estrogens mechanism; mechanism estrogens; metab estrogens  
IT Estrogenic hormones  
RL: BIOL (Biological study)  
(carcinogenesis in relation to)  
IT Neoplasms, metabolism  
(of estrogens in induced mammary)  
IT 50-27-1 50-28-2, biological studies 4954-12-5 5635-50-7  
RL: BIOL (Biological study)  
(in reproductive tract of female after administration)  
IT 4954-12-5  
RL: BIOL (Biological study)  
(in reproductive tract of female after administration)  
RN 4954-12-5 HCAPLUS  
CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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=&gt; fil hcaold

FILE 'HCAOLD' ENTERED AT 11:46:26 ON 29 MAY 2002

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L64 ANSWER 1 OF 3 HCAOLD COPYRIGHT 2002 ACS

AN CA64:8257g CAOLD

TI 17.beta.-estradiol 17-methyl ether

AU Coombs, M. M.; Roderick, H. R.

TI orientation of the fragmentation in mass spectrometry by the introduction of functional groups - (VII) ethylene ketals of 2-oxosteroids

AU Audier, Henri; Fetizon, M.; Gramain, J. C.

IT 700-77-6 1743-60-8 4832-17-1 4953-96-2 4954-12-5

4954-13-6 4954-14-7 4954-16-9 4954-17-0 4967-93-5 4967-94-6

4967-96-8 4967-97-9 4968-11-0 4999-72-8 5380-79-0 5506-56-9

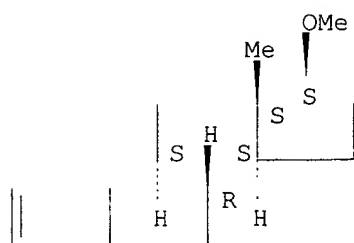
6857-86-9

IT 4954-12-5

RN 4954-12-5 HCAOLD

CN Estra-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

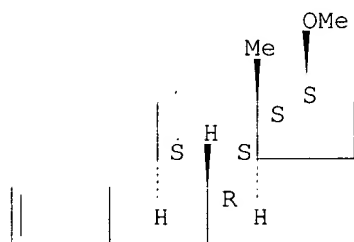
Absolute stereochemistry.



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L64 ANSWER 2 OF 3 HCAOLD COPYRIGHT 2002 ACS  
 AN CA61:16379g CAOLD  
 TI fractionation of estrogen methyl esters with Al2O3 column chromatography-estn. of of 16-epiestriol in pregnancy urine  
 AU Shida, Keizo; Kimura, N.; Kambegawa, A.  
 IT 1474-53-9 3434-79-5 4954-12-5  
 IT 4954-12-5  
 RN 4954-12-5 HCAOLD  
 CN Estr-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

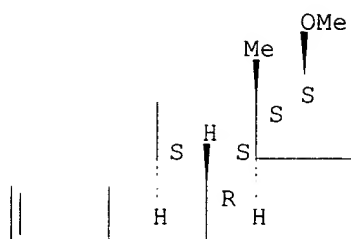
Absolute stereochemistry.



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L64 ANSWER 3 OF 3 HCAOLD COPYRIGHT 2002 ACS  
 AN CA56:7630a CAOLD  
 TI steroid derivs. - (XII) chromatography of neutral steroids on a thin Al2O3 layer  
 AU Hermanek, Stanislav; Schwarz, V.; Cekan, Z.  
 IT 113-38-2 604-32-0 633-34-1 809-51-8 1061-54-7 1169-49-9  
 1175-12-8 1182-65-6 1235-98-9 1255-57-8 1259-22-9 1639-43-6  
 1639-44-7 1807-15-4 2080-86-6 2088-71-3 2099-26-5 3604-60-2  
 4139-90-6 4651-48-3 4860-15-5 4954-12-5 6252-45-5  
 14072-39-0 14546-23-7 19637-35-5 20272-84-8 20867-15-6 23838-12-2  
 29163-23-3 29789-88-6 31823-53-7 33854-98-7 34209-81-9 41329-03-7  
 50303-03-2 71205-59-9 82979-88-2 95557-72-5 95908-73-9 96273-79-9  
 96275-23-9 96345-96-9 96391-62-7 96553-92-3 96772-72-4 107158-49-6  
 IT 4954-12-5  
 RN 4954-12-5 HCAOLD  
 CN Estr-1,3,5(10)-trien-3-ol, 17-methoxy-, (17.beta.)- (9CI) (CA INDEX NAME)

Absolute stereochemistry.



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L68 ANSWER 1 OF 3 HCAPLUS COPYRIGHT 2002 ACS

AN 1966:44062 HCAPLUS

DN 64:44062

OREF 64:8257f-g

TI 17.beta.-Estradiol 17-methyl ether

AU Coombs, M. M.; Roderick, H. R.

CS Imp. Cancer Res. Fund, Lincoln's Inn Fields, London

SO Steroids (1965), 6(6), 841-4

DT Journal

LA English

CC 42 (Steroids)

AB Exptl. results and characterization of various products of 17.beta.-estradiol 17-Me ether are presented.

L68 ANSWER 2 OF 3 HCAPLUS COPYRIGHT 2002 ACS

AN 1964:493831 HCAPLUS

DN 61:93831

OREF 61:16379g-h

TI Fractionation of estrogen methyl esters and alumina column chromatography (estimation of 16-epiestriol in pregnancy urine)

AU Shida, K.; Kimura, M.; Kanbegawa, A.

CS Med. and Dental Univ. School Med., Tokyo

SO Nippon Naibumpi Gakkai Zasshi (1961), 37(1), 5-9

DT Journal

LA Unavailable

CC 58 (Hormones)

AB After boiling for 15 min. with 15% concd. HCl, late pregnancy urine was extd. twice with ether, washed with 5% NaHCO<sub>3</sub> and water, dried with anhyd. Na<sub>2</sub>SO<sub>4</sub>, and concd, to about 10 ml. in a water bath. The estrogens were extd. with benzene-petr. ether and reextd. with 1.6% NaOH. H<sub>3</sub>BO<sub>3</sub> and dimethyl sulfate were added followed by stirring for 30 min. Following the addn. of 30% H<sub>2</sub>O<sub>2</sub> the methylated estrogens were chromatographed on an alumina column 0.5 .times. 20 cm. prepd. by partial filling with petr. ether and the addn. of 2.0 g. of Brockmann alumina at 18.degree. under 10-12 mm. Hg. The Me esters of estrone, estradiol, 16-epiestriol, and estriol were eluted with 40% petr. ether in benzene, 1.0% MeOH in benzene, and 3.0% MeOH in benzene, resp. The content of 16-epiestriol reached 11.5% in late pregnancy urine. From Abstr. Japan. Med. 1(15), Abstr. No. 6640(1961).

L68 ANSWER 3 OF 3 HCAPLUS COPYRIGHT 2002 ACS

AN 1962:40001 HCAPLUS

DN 56:40001

OREF 56:7630a-d

TI Steroid derivatives. XII. Chromatography of neutral steroids on a thin aluminum oxide layer

AU Hermanek, S.; Schwarz, V.; Cekan, Z.  
 CS Research Inst. Nat. Drugs, Prague  
 SO Collection Czechoslov. Chem. Commun. (1961), 26, 1669-79  
 DT Journal  
 LA German  
 CC 55 (Biochemical Methods)  
 AB cf. CA 55, 27411c; 56, No. 5.-The use of Al<sub>2</sub>O<sub>3</sub> without binder has the advantage of simplicity in prepg. a thin layer for chromatography. Alk. Al<sub>2</sub>O<sub>3</sub> was used with ligroin (b. 30-50.degree.), benzene, ligroinbenzene, and benzene-EtOH mixts. in various proportions. .DELTA.4-3-Ketones were detected by lightly spraying with SbCl<sub>3</sub> in CHCl<sub>3</sub>, other .DELTA.4-substances with SbCl<sub>3</sub> in CHCl<sub>3</sub> with 10% SOCl<sub>2</sub>. Alky. of Al<sub>2</sub>O<sub>3</sub> was without influence on R<sub>f</sub> values and, except for formates, trichloroacetates, and trifluoroacetates, did not degrade the substances during the 10-20 min. of development. Benzene was used as the first solvent for unknown mixts. R<sub>f</sub> values in several solvents are tabulated for some 90 steroids belonging to 3-substituted cholest-5-enes, 17-substituted 3.beta.-acetoxyandrost-5-enes, 3.beta.substituted androst-5-en-17-ones, 3.beta.-substituted methyl-7keto-eti-5-enates, 3.beta.-substituted cholest-5-en-7-ones, 17.beta.substituted androst-4-en-3-ones, and miscellaneous classes. Chromatographic control of prepn. and purity of a substance is exemplified by the sepn. of pregn-4-ene-17.alpha.,21-diol-3,20-dione, its diacetates, 17.alpha.,21-diacetoxypregn-5-en-3.beta.-ol-20-one, and 17.alpha.,21-diacetoxy-3.beta.-formyloxypregn-5-en-20-one and accompanying impurities. Adsorptivity of 17.beta.-substituents increased in the following order: COOCH<sub>3</sub>, OBz, CN-COOCH<sub>3</sub>, OAc, O, OH; for 3.beta.-substituents of cholest-5-ene the order was: H, Cl, OCH<sub>3</sub>, OAc, OH, and NMe<sub>2</sub>; similarly, cyclohexylamine moved more slowly than cyclohexanol while aniline was much faster than PhOH.

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(FILE 'REGISTRY' ENTERED AT 11:09:26 ON 29 MAY 2002)  
 DEL HIS

FILE 'HCAPLUS' ENTERED AT 11:09:34 ON 29 MAY 2002

E PROKAI L/AU  
 L1 89 S E3,E4  
 L2 1 S E7  
 E SIMPKINS J/AU  
 L3 227 S E3,E5,E7-E9  
 L4 22 S L1-L3 AND STERO?/SC,SX,CW  
 L5 123 S L1-L3 AND (?ESTROGEN? OR ?ESTRADIOL? OR ?STEROID?)  
 L6 126 S L4,L5  
 L7 8 S L1,L2 AND L3  
 L8 3 S L7 AND L4-L6  
 L9 0 S L6 AND ALKYLEETHER  
 L10 2 S L6 AND ALKYL(L)ETHER  
 L11 2 S L10 AND L1-L10  
 SEL RN

FILE 'REGISTRY' ENTERED AT 11:12:06 ON 29 MAY 2002

L12 18 S E1-E18  
 L13 16 S L12 AND NR>=4  
 L14 5 S L13 AND (C22H32O2 OR C24H36O2 OR C26H40O2)  
 L15 3 S L14 NOT 3() (BUTOXY OR OCTYLOXY)  
 L16 777 S (C22H32O2 OR C24H36O2 OR C26H40O2)/MF AND C5-C6-C6-C6/ES  
 L17 110 S L16 AND 4432.3.65/RID AND 4/NR  
 L18 104 S L17 NOT 3 OL  
 L19 6 S L17 NOT L18  
 L20 5 S L19 NOT 13C#  
 L21 5 S L15,L20

SEL RN  
L22 0 S E19-E23/CRN

FILE 'HCAOLD' ENTERED AT 11:20:06 ON 29 MAY 2002  
L23 0 S L21

FILE 'USPATFULL, USPAT2' ENTERED AT 11:20:07 ON 29 MAY 2002  
L24 1 S L21

FILE 'HCAPLUS' ENTERED AT 11:20:18 ON 29 MAY 2002  
L25 8 S L21  
L26 3 S L1-L3 AND L25  
L27 8 S L25,L26

FILE 'REGISTRY' ENTERED AT 11:20:53 ON 29 MAY 2002

FILE 'USPATFULL, USPAT2' ENTERED AT 11:21:06 ON 29 MAY 2002

FILE 'HCAPLUS' ENTERED AT 11:21:16 ON 29 MAY 2002

FILE 'REGISTRY' ENTERED AT 11:21:39 ON 29 MAY 2002

L28 STR  
L29 0 S L28 SAM  
L30 STR L28  
L31 21 S L30 SAM  
L32 4506 S L30 FUL  
SAV TEMP L32 QAZI893324/A  
L33 3917 S L32 AND 4432.3.65/RID  
L34 589 S L32 NOT L33  
L35 STR L28  
L36 5 S L35 CSS SAM SUB=L32  
L37 642 S L32 NOT ESTRA?  
L38 314 S L37 NOT ?PREGN?/CNS  
L39 86 S L38 NOT GONA?  
L40 48 S L39 NOT CHOL?  
L41 3864 S L32 NOT L37-L40  
L42 3 S L32 NOT CN/FA  
L43 5 S L35 CSS SAM SUB=L41  
L44 100 S L35 CSS FUL SUB=L41  
SAV TEMP L44 QAZI893324A/A  
L45 95 S L44 NOT L21  
L46 93 S L45 NOT (ION OR LABELED OR (D OR T)/ELS OR 11C# OR 13C# OR 14  
L47 22 S L46 AND 4/NR  
L48 3 S L47 AND (C21H28O2 OR C21H26O2 OR C21H30O2)  
L49 STR L35  
L50 0 S L49 CSS SAM SUB=L32  
L51 15 S L49 CSS FUL SUB=L32  
SAV L51 TEMP QAZI893324B/A  
L52 13 S L51 NOT (13C# OR T/ELS)  
L53 8 S L48,L52 NOT L21

FILE 'HCAOLD' ENTERED AT 11:38:33 ON 29 MAY 2002  
L54 0 S L53

FILE 'HCAPLUS' ENTERED AT 11:38:36 ON 29 MAY 2002  
L55 10 S L53

FILE 'USPATFULL, USPAT2' ENTERED AT 11:38:41 ON 29 MAY 2002  
L56 1 S L53

FILE 'REGISTRY' ENTERED AT 11:38:55 ON 29 MAY 2002

FILE 'USPATFULL, USPAT2' ENTERED AT 11:39:21 ON 29 MAY 2002

L57 FILE 'HCAPLUS' ENTERED AT 11:39:34 ON 29 MAY 2002  
25 S L32 AND L1-L3  
SEL HIT RN

L58 FILE 'REGISTRY' ENTERED AT 11:40:22 ON 29 MAY 2002  
41 S E24-E64  
L59 37 S L58 NOT L21,L53  
L60 23 S L59 NOT (ESTER OR OATE)  
L61 18 S L60 NOT CARBOXYLATE  
L62 14 S L61 NOT ?OATE?/CNS  
L63 11 S L62 NOT (ACETATE OR 17 17 DIMETHOXY)

L64 FILE 'HCAOLD' ENTERED AT 11:45:14 ON 29 MAY 2002  
3 S L63

L65 FILE 'HCAPLUS' ENTERED AT 11:45:28 ON 29 MAY 2002  
17 S L63

L66 FILE 'USPATFULL, USPAT2' ENTERED AT 11:45:34 ON 29 MAY 2002  
4 S L63

FILE 'REGISTRY' ENTERED AT 11:45:42 ON 29 MAY 2002

FILE 'USPATFULL, USPAT2' ENTERED AT 11:45:59 ON 29 MAY 2002

FILE 'HCAPLUS' ENTERED AT 11:46:09 ON 29 MAY 2002

FILE 'HCAOLD' ENTERED AT 11:46:26 ON 29 MAY 2002  
SEL AN L64  
EDIT /AN /OREF

L67 FILE 'HCAPLUS' ENTERED AT 11:47:03 ON 29 MAY 2002  
6 S E65-E67  
L68 3 S L67 NOT (AUDIER H? OR FUTTERWEIT W? OR SANNO Y?)/AU